

DESCRIPTION

Cephem Compounds having broad antibacterial spectrum

Technical Field

5 The present invention relates to cephem compounds having a broad antibacterial spectrum over various pathogenic bacteria and pharmaceutical compositions containing the same, as well as a production method and intermediates therefor. The compounds of the present invention are stable against β -lactamase and efficacious against β -lactamase-producing cephem-resistant bacteria including *Pseudomonas*
10 *aeruginosa*.

Background

Study of so-called broad spectrum cephem compounds having potent antibacterial activities against various Gram-positive and Gram-negative bacteria has
15 recently been focused on cephem compounds wherein the 7-side chain is substituted with aminothiazole or aminothiadiazaole and the 3-position with a cyclic-type quarternary ammoniummethyl group. For example, the known 7-aminothiazole types include cefepime hydrochloride (USP 4,406,899), cefpirome sulfate (USP 4,609,653, JP(A) S57-192394), and cefoselis sulfate (JP(A) H07-196665, WO97/41128),
20 and the 7-aminothiadiazaole types include cefclidin (USP 4,748,171), and cefozopran hydrochloride (USP 4,864,022, JP(A) S62-149682, JP(A) H03-47189). Such types of cephem compounds are also reported in JP Patent publication (Kokai) S-58-4789 which discloses compounds having an "optionally substituted 2 or more of N atoms-containing heterocycle cation group" at the 3-position and in JP Patent publication
25 (Kokai) S-60-155183 which discloses compounds having a "2 or more of N atoms-containing unsaturated condensed heterocyclic cation group" at the 3-position.

Documents such as JP Patent publication (Kokai) S-60-97982, JP Patent publication (Kokai) S-59-130294, JP Patent publication (Kokai) S-60-34973, JP Patent publication (Kokai) S-62-114990, JP Patent publication (Kokai) S-64-42491, and
30 WO87/06232 etc. disclose cephem compounds which have a halogen on an aminothiazole ring at the 7-position or which are substituted with COOH at the end of the oxime part on the 7-side chain. These documents do not disclose a cephem compound having the both structural characteristics.

A cephem compound, which has a halogen on an aminothiazole ring at the 7-
35 position and is substituted with COOH at the end of the oxime part on the 7-side chain,

is known in JP Patent publication (Kokai) S-60-231684. However, a specifically disclosed compound is that wherein the methylene group bonding to the oxime part on the 7-side chain is non-substituted or dimethyl-substituted type. JP Patent publication (Kokai) S-57-131794 and JP Patent publication (Kokai) H-1-308286 discloses compounds wherein the methylene group bonding to the oxime part on the 7-side chain is substituted with monomethyl, however, the configuration is not specified and a quarternary ammonium group is not disclosed as a possible substituent on the methylene group at the 3-position. Further, any antibacterial activities against cephem-resistant *Pseudomonas aeruginosa* are not described therein.

A cephem compound having a quarternary ammonium group at the 3-position and a side chain of aminothiazole / oxime type at the 7-position, so-called broad spectrum antibacterial-type cephem, is known as being efficacious against G(-) bacteria including *Pseudomonas aeruginosa*. For example, ceftazidime has been reported as being stable against β -lactamase and possessing a relatively potent activity against β -lactamase-producing *Pseudomonas aeruginosa* (*Acta Microbiologica Hungarica* 35 (4), pp. 327-359 (1988)).

Under the above circumstances, among G(-) bacteria, the number of bacteria resistant to some broad spectrum antibacterial-type cepheims has recently increased. The frequency of clinical isolation of cephem-resistant *Pseudomonas aeruginosa*, which highly produce β -lactamase, esp. Class C-type β -lactamase, has raised, which is recognized as a social problem worldwide ("Classification and Epidemiology of Recent β -lactamase", *Clinic and Microorganism* Vol.26 No.2 1999.3 P103-109). However, a cephem compound with a potent activity against such cephem-resistant *Pseudomonas aeruginosa* has not been reported.

Therefore, the development of a novel cephem compound with broad antibacterial spectrum, preferably a compound possessing a potent activity against cephem-resistant *Pseudomonas aeruginosa* which produce β -lactamase has been desired. In preference, such a compound is useful as an injection.

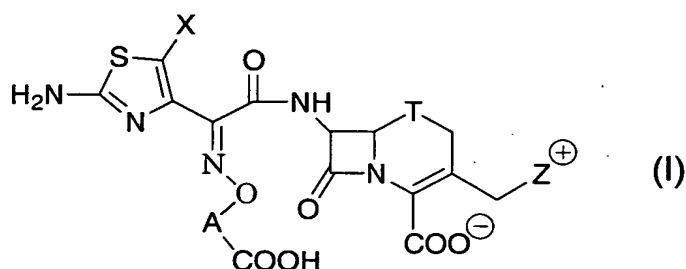
Disclosure of the Invention

The present inventors have found that the stability of a cephem compound against β -lactamase produced by cephem-resistant *Pseudomonas aeruginosa* can be improved so as to enhance the antibacterial activity against such *Pseudomonas aeruginosa*, by means of introducing a halogen atom or the like into an aminothiazole ring on the 7-side chain, a carboxyl group into the end of the oxime group bonding to the carbon

atom at α -position, and an N-containing heterocyclic group, preferably a quarternary ammonium group into the 3-position, respectively.

As a more preferable embodiment, the inventors have found that the antibacterial activity can further be enhanced by introducing a lower alkyl, preferably methyl as α -configuration into the methylene group, whereby to accomplish the present invention shown below.

1. A compound of the formula :



(wherein,

T is S, SO or O ;

X is halogen, CN, carbamoyl optionally substituted with lower alkyl, lower alkyl, lower alkoxy, or lower alkylthio ;

A is substituted lower alkylene (wherein the substituent is optionally substituted mono lower alkyl, optionally substituted lower alkylidene, or optionally substituted lower alkylene) ;

Z^+ is an optionally substituted, a cation and an N atom-containing heterocyclic group), ester, amino-protected compound wherein the amino bonds to a thiazole ring at the 7-position, or pharmaceutically acceptable salt or solvate thereof.

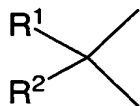
2. A compound according to the above 1 wherein T is S, ester, amino-protected compound wherein the amino bonds to a thiazole ring at the 7-position, or pharmaceutically acceptable salt or solvate thereof.

3. A compound according to the above 1 wherein T is O, ester, amino-protected compound wherein the amino bonds to a thiazole ring at the 7-position, or pharmaceutically acceptable salt or solvate thereof.

4. A compound according to the above 1 wherein X is halogen or lower alkyl, ester, amino-protected compound wherein the amino bonds to a thiazole ring at the 7-

position, or pharmaceutically acceptable salt or solvate thereof.

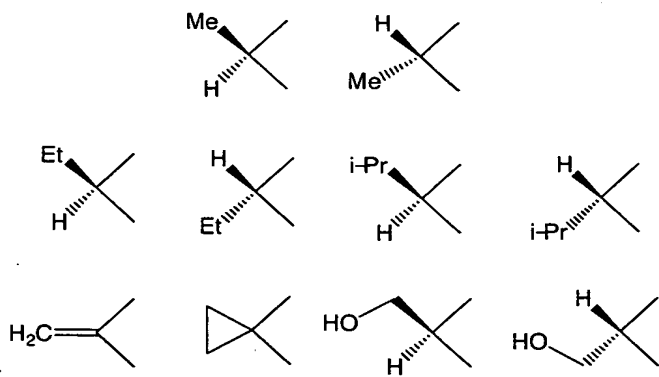
5. A compound according to the above 1 wherein A is of the formula :



5 (wherein, R¹ and R² are different each other and independently hydrogen or optionally substituted lower alkyl, or taken together may form optionally substituted lower alkylidene or optionally substituted lower alkylene.), ester, amino-protected compound wherein the amino bonds to a thiazole ring at the 7-position, or pharmaceutically acceptable salt or solvate thereof.

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6. A compound according to the above 5 wherein A is a divalent group of any of the following formulae, ester, amino-protected compound wherein the amino bonds to a thiazole ring at the 7-position, or pharmaceutically acceptable salt or solvate thereof.



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(wherein, Me is methyl ; Et is ethyl ; i-Pr is isopropyl)

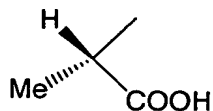
7. A compound according to the above 5 wherein R¹ and R² are different each other and independently hydrogen or lower alkyl, ester, amino-protected compound wherein the amino bonds to a thiazole ring at the 7-position, or pharmaceutically acceptable salt or solvate thereof.

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8. A compound according to the above 5 wherein R¹ and R² are different each other and independently hydrogen or methyl, ester, amino-protected compound wherein the amino bonds to a thiazole ring at the 7-position, or pharmaceutically acceptable salt or solvate thereof.

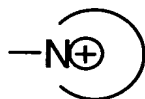
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9. A compound according to the above 5 wherein "-A-COOH" is a group of the formula:



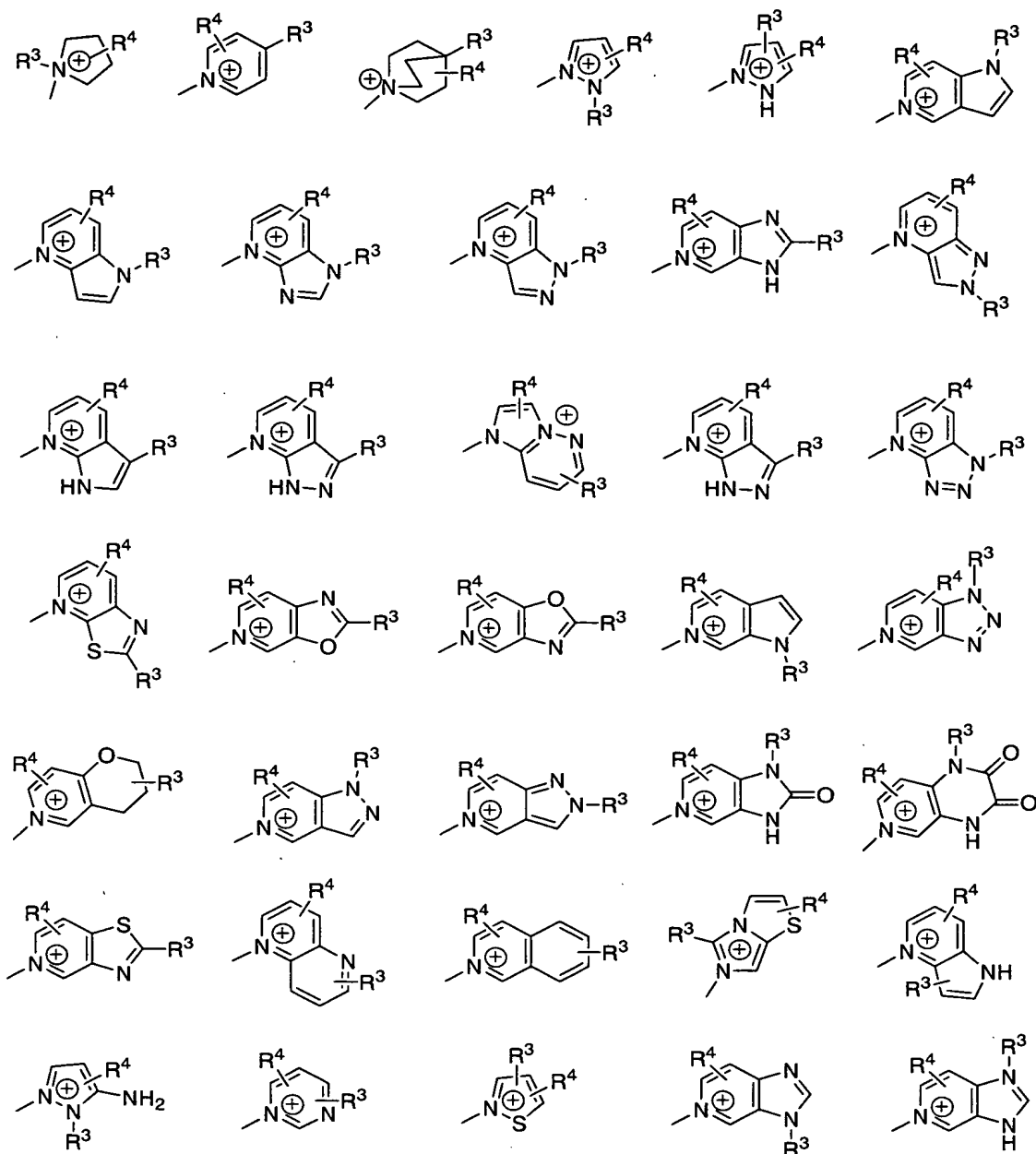
5 ester, amino-protected compound wherein the amino bonds to a thiazole ring at the 7-position, or pharmaceutically acceptable salt or solvate thereof.

10. A compound according to the above 1 wherein Z^+ is a saturated or unsaturated, monocyclic or condensed cyclic, and at least one or more of N atoms-containing quarternary ammonium group of the formula :



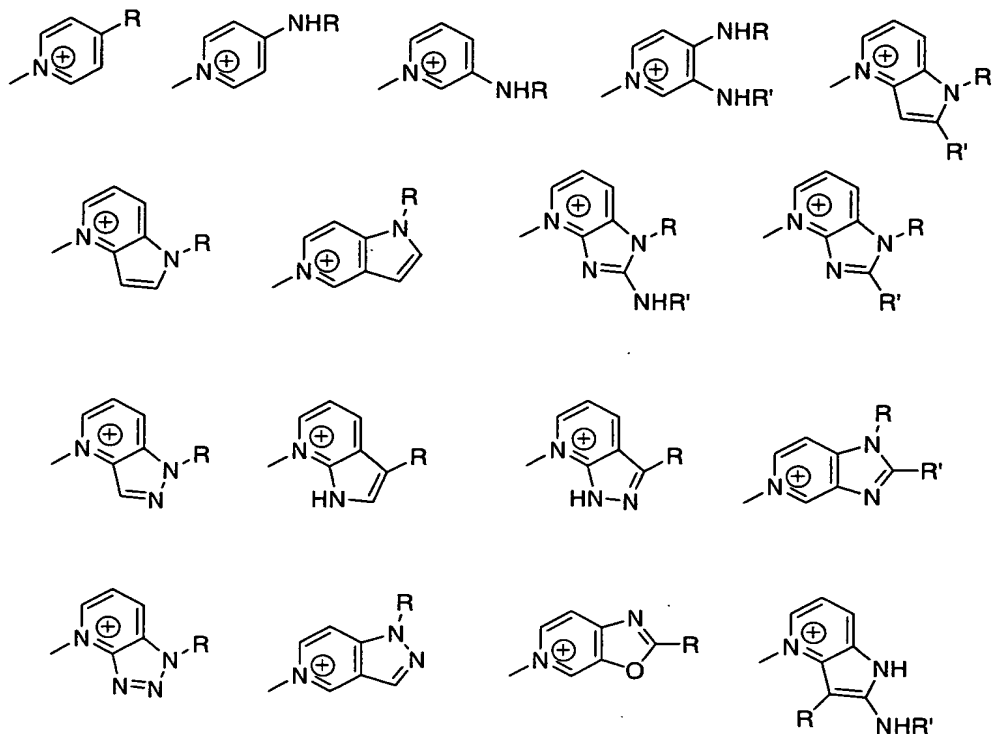
10 which may have 1 to 4 substituents, ester, amino-protected compound wherein the amino bonds to a thiazole ring at the 7-position, or pharmaceutically acceptable salt or solvate thereof.

15 11. A compound according to the above 1, ester, amino-protected compound wherein the amino bonds to a thiazole ring at the 7-position, or pharmaceutically acceptable salt or solvate thereof, wherein Z^+ is a heterocyclic group of any one of the formulae:



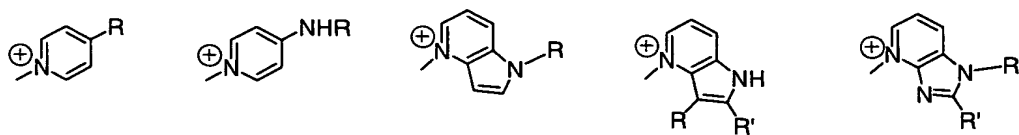
(wherein, R^3 and R^4 each is independently hydrogen, optionally substituted lower alkyl, optionally substituted cycloalkyl, optionally substituted lower alkenyl, optionally substituted amino, hydroxy, halogen, optionally substituted carbamoyl, optionally substituted alkyloxy, or optionally substituted heterocyclic group.)

12. A compound according to the above 1, ester, amino-protected compound wherein the amino bonds to a thiazole ring at the 7-position, or pharmaceutically acceptable salt or solvate thereof, wherein Z^+ is a heterocyclic group of any one of the formulae:



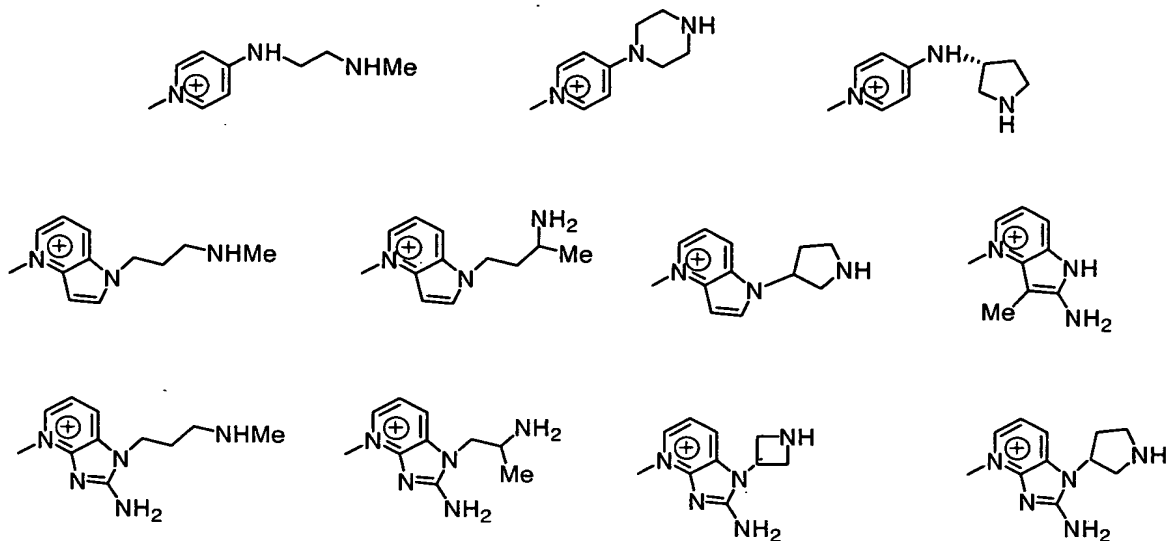
(wherein, R and R' each is independently hydrogen, lower alkyl, amino, mono- or di-
 lower alkylamino, lower alkenyl, amino lower alkyl, lower alkylamino lower alkyl,
 5 lower alkylamino lower alkylamino, amino lower alkyloxyamino, amino substitute
 with optionally substituted heterocyclic group, hydroxy lower alkyl, hydroxy lower
 alkylamino lower alkyl, lower alkoxy lower alkyl, carbamoyl lower alkyl, carboxy lower
 alkyl, lower alkylcarbonylamino lower alkyl, lower alkoxy carbonylamino lower alkyl,
 lower alkyloxy, the other various optionally substituted lower alkyl, lower alkyl having
 10 2 kinds of substituents, or optionally substituted heterocyclic group.)

13. A compound according to the above 1, ester, amino-protected compound wherein
 the amino bonds to a thiazole ring at the 7-position, or pharmaceutically acceptable
 salt or solvate thereof, wherein Z^+ is a heterocyclic group of any one of the formulae:



(wherein, R is independently hydrogen, lower alkyl, amino lower alkyl, lower
 alkylamino lower alkyl, amino substituted with optionally substituted heterocyclic
 group, or optionally substituted heterocyclic group ; R' is amino.)

14. A compound according to the above 1, ester, amino-protected compound wherein the amino bonds to a thiazole ring at the 7-position, or pharmaceutically acceptable salt or solvate thereof, wherein Z^+ is a heterocyclic group of any one of the formulae:



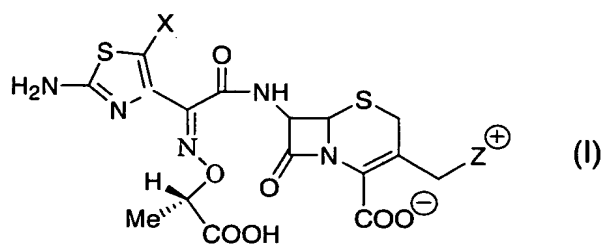
(wherein, Me is methyl.)

15. A compound according to the above 1, ester, amino-protected compound wherein the amino bonds to a thiazole ring at the 7-position, or pharmaceutically acceptable salt or solvate thereof, wherein T is S ; X is halogen ; A is a divalent group shown in any of the above 5 to 9 ; Z^+ is a heterocyclic group shown in any of the above 10 to 14.

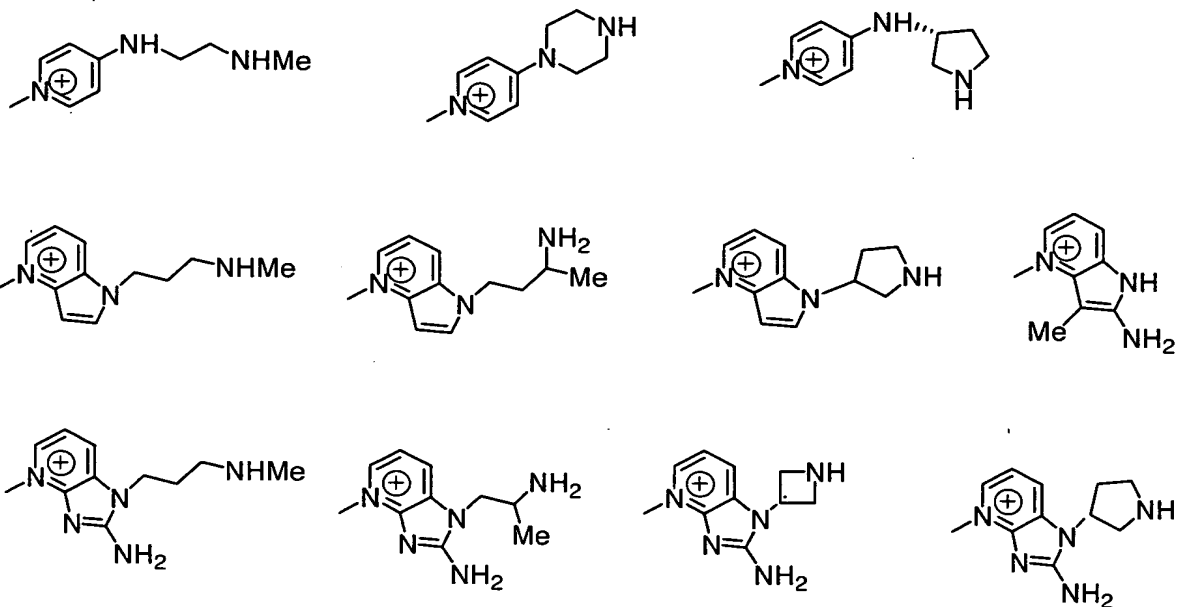
16. A compound according to the above 1, ester, amino-protected compound wherein the amino bonds to a thiazole ring at the 7-position, or pharmaceutically acceptable salt or solvate thereof, wherein T is S ; X is halogen ; A is a divalent group shown in the above 8 ; Z^+ is a heterocyclic group shown in the above 12.

17. A compound according to the above 1, ester, amino-protected compound wherein the amino bonds to a thiazole ring at the 7-position, or pharmaceutically acceptable salt or solvate thereof, wherein T is S ; X is halogen ; A is a divalent group shown in the above 9 ; Z^+ is a heterocyclic group shown in the above 13 or 14.

18. A compound according to the above 1 of the following formula, or pharmaceutically acceptable salt or solvate thereof.



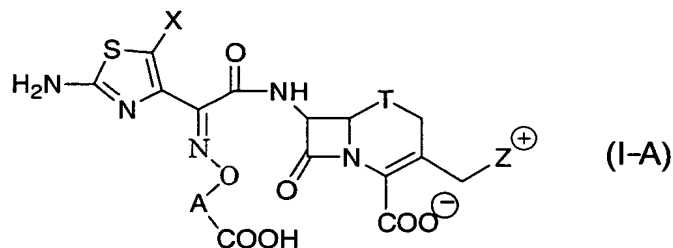
(wherein, X is halogen ; Z^+ is a heterocyclic group of any of the formulae)



5

(wherein, Me is methyl)

19. A compound of the formula :



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(wherein,

T is S, SO or O ;

X is halogen, CN, carbamoyl optionally substituted with lower alkyl, lower alkyl, lower alkoxy, or lower alkylthio ;

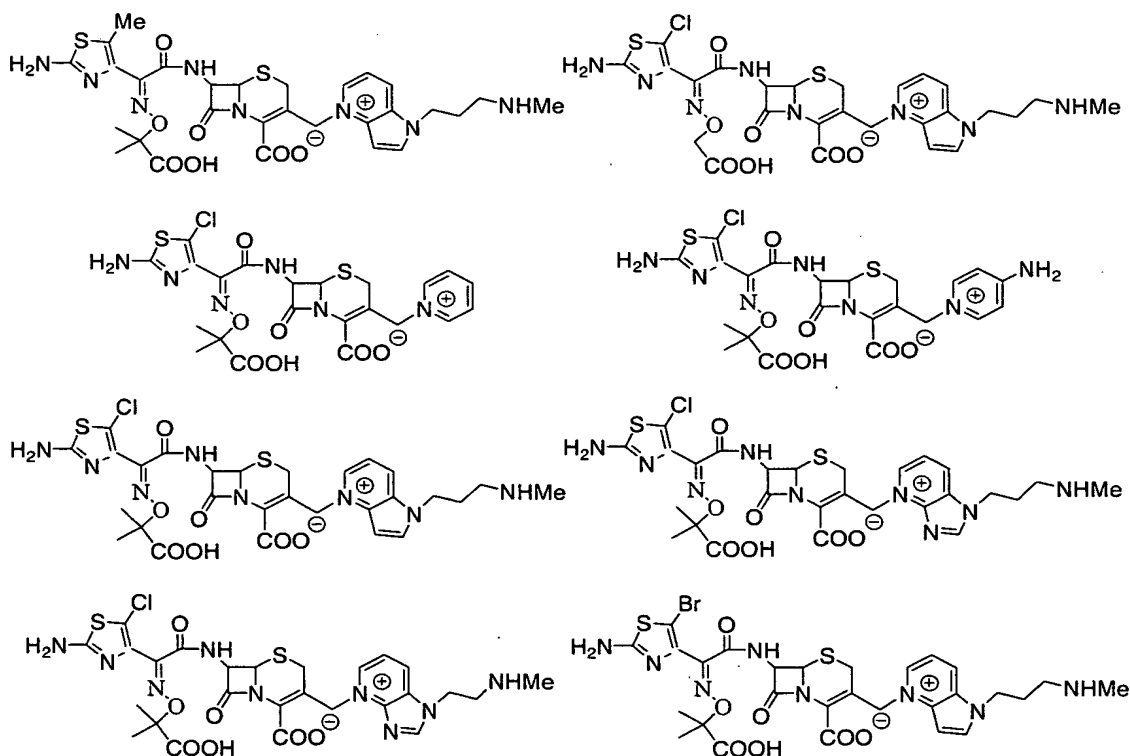
A is optionally substituted lower alkylene (excluding that the substituent is optionally substituted mono lower alkyl, optionally substituted lower alkylidene, or optionally substituted lower alkylene) ;

Z⁺ is optionally substituted, a cation- and an N atom-containing heterocyclic group),

- 5 ester, amino-protected compound wherein the amino bonds to a thiazole ring at the 7-position, or pharmaceutically acceptable salt or solvate thereof, excluding that T is S ; X is halogen and 1) A is methylene ; Z⁺ is pyridinium or 2) A is dimethylmethylene ; Z⁺ is imidazo[1, 2-a]pyridinium).

- 10 20. A compound of the above 19, ester, amino-protected compound wherein the amino bonds to a thiazole ring at the 7-position, or pharmaceutically acceptable salt or solvate thereof, wherein T is S, X is halogen or lower alkyl ; A is methylene optionally substituted with di-lower alkyl.

- 15 21. A compound of the above 20, ester, amino-protected compound wherein the amino bonds to a thiazole ring at the 7-position, or pharmaceutically acceptable salt or solvate thereof, of any of the formula:

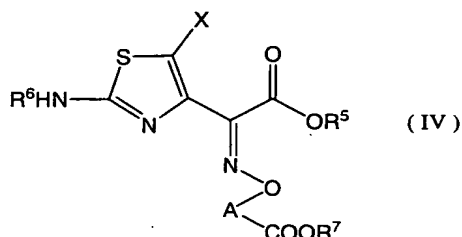


- 20 22. A pharmaceutical composition containing a compound of the above 1 to 21, ester,

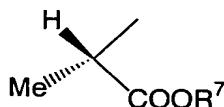
amino-protected compound wherein the amino bonds to a thiazole ring at the 7-position, or pharmaceutically acceptable salt or solvate thereof.

23. An antibacterial composition containing a compound of the above 1 to 21, ester,
5 amino-protected compound wherein the amino bonds to a thiazole ring at the 7-position, or pharmaceutically acceptable salt or solvate.

24. A compound or pharmaceutically acceptable salt, of the formula :



- 10 (wherein, X is halogen, CN, carbamoyl optionally substituted with lower alkyl, lower alkyl, lower alkoxy, or lower alkylthio ; A is of the formula :



R⁵ is hydrogen or carboxy-protecting group ; R⁶ is hydrogen or amino-protecting group ; R⁷ is hydrogen or carboxy-protecting group)

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25. A compound or pharmaceutically acceptable salt according to the above 24, wherein X is halogen or lower alkyl.

26. A compound or pharmaceutically acceptable salt according to the above 24,
20 wherein X is halogen.

Further, the present invention provides a method for preparing the invention compounds and intermediates thereof, as well as a method for prevention or treatment of bacterial infection by administering the invention compound, and use of the
25 invention compound for preparing an antibacterial agent.

Best Mode for Carrying Out the Invention

Terms used herein are explained below. Unless otherwise mentioned, each term, by itself or as part of another, has the following meaning.

(Definition of T)

T is S, SO or O, preferably S or O, and more preferably S.

(Definition of X)

5 X is halogen, CN, carbamoyl optionally substituted with lower alkyl, lower alkyl, lower alkoxy, or lower alkylthio.

Halogen includes F, Cl, and Br, preferably Cl or Br, and more preferably Cl.

10 Examples of lower alkyl include a straight or branched C1 to C6 alkyl such as methyl, ethyl, n-propyl, i-propyl, t-butyl, n-pentyl, and n-hexyl, and preferably is C1 to C3 alkyl, and more preferably is methyl.

Examples of lower alkoxy include oxy bonding to lower alkyl, such as methoxy, ethoxy, n-propoxy, i-propoxy, t-butoxy, n-pentyloxy, and n-hexyloxy, preferably C1 to C3 alkoxy, and more preferably methoxy.

15 Examples of lower alkylthio include thio bonding to the lower alkyl, such as methylthio, ethylthio, n-propoxy, i-propylthio, t-butylthio, n-pentylthio, and n-hexylthio, preferably C1 to C3 alkylthio, and more preferably methylthio.

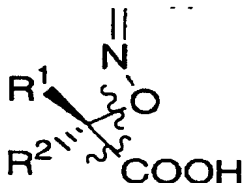
X is preferably halogen (e.g., Cl, Br) or lower alkyl (e.g., methyl), more preferably halogen.

20 (Definition of A)

A can be any of divalent groups which does not bring a negative effect into the antibacterial activity of compound (I) or compound (I-A), and preferably A is lower alkylene optionally substituted with R¹, R² or the like. In compound (I), A is substituted lower alkylene.

25 The lower alkylene is a divalent group derived from the above-mentioned lower alkyl, preferably C1 to C3 alkylene, more preferably methylene (-CH₂-).

A is more preferably methylene substituted with the following R¹ and R², and preferably A is of the following configuration.



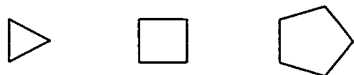
(Definition of R^1 , R^2)

R^1 and R^2 are each independently hydrogen, optionally substituted lower alkyl, or taken together may form optionally substituted lower alkylidene or optionally substituted lower alkylene, provided that in compound (I), R^1 and R^2 are different each other.

The lower alkyl includes the above-mentioned lower alkyl, preferably C1 to C4 alkyl, more preferably methyl, ethyl, or propyl (e.g., n-propyl, i-propyl), and most preferably methyl.

The lower alkylidene includes a divalent group which is derived from the above lower alkyl by deducting two hydrogens bonding to the same carbon atom, for example, $=CH_2$, $=CHCH_3$, $=CHCH_2CH_3$, $=C(CH_3)_2$, $=CHC(CH_3)_3$, preferably $=CH_2$, $=CHCH_3$, or $=C(CH_3)_2$, and more preferably $=CH_2$.

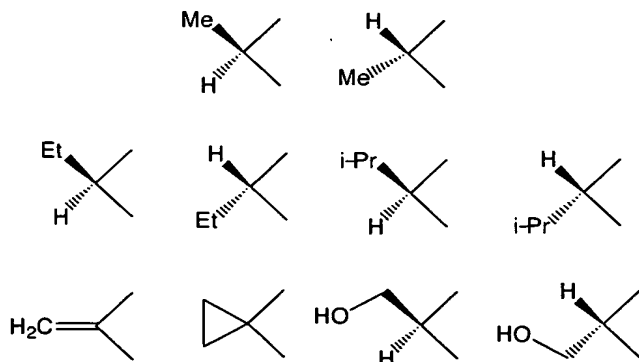
The lower alkylene includes $-(CH_2)_n$ (n is an integer from 2 to 4, preferably 2). R^1 and R^2 taken together may form lower alkylene, which taken together with the neighboring carbon atom can form the following cycloalkyl, preferably cyclopropyl or cyclobutyl, and more preferably cyclopropyl.



When the above lower alkyl, lower alkylidene, or lower alkylene is substituted, the substituents include halogen (e.g., F, Cl), hydroxy, lower alkoxy (e.g., methoxy, ethoxy), and preferably hydroxy.

The combination of (R^1 , R^2) is preferably, (methyl, hydrogen), (hydrogen, methyl), or (methyl, methyl) or taken together may form $=CH_2$, $-(CH_2)_2$ etc. In compound (I), more preferred is hydrogen and lower alkyl, most preferred is (R^1 , R^2)=(methyl, hydrogen), or (hydrogen, methyl). Particularly preferred is (hydrogen, methyl).

In compound (I), preferred are the following divalent groups.

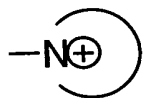


(wherein, Me is methyl ; Et is ethyl ; i-Pr is isopropyl.)

(Definition of Z⁺)

Z⁺ is an optionally substituted, a cation- and N-containing heterocyclic group.
5 Unless the pharmacological activity is negatively influenced, the number and position of the substituent, the kind of cation, and the kind of heterocycle can be of variety. Z⁺ includes various kinds of groups which are well known to or readily recognized by a skilled person in the invention field as a heterocyclic group at the 3-position of cephem compounds. The cation preferably locates around the N atom neighboring to the 3-
10 methylene of compound (I).

Z⁺ is preferably of the formula :



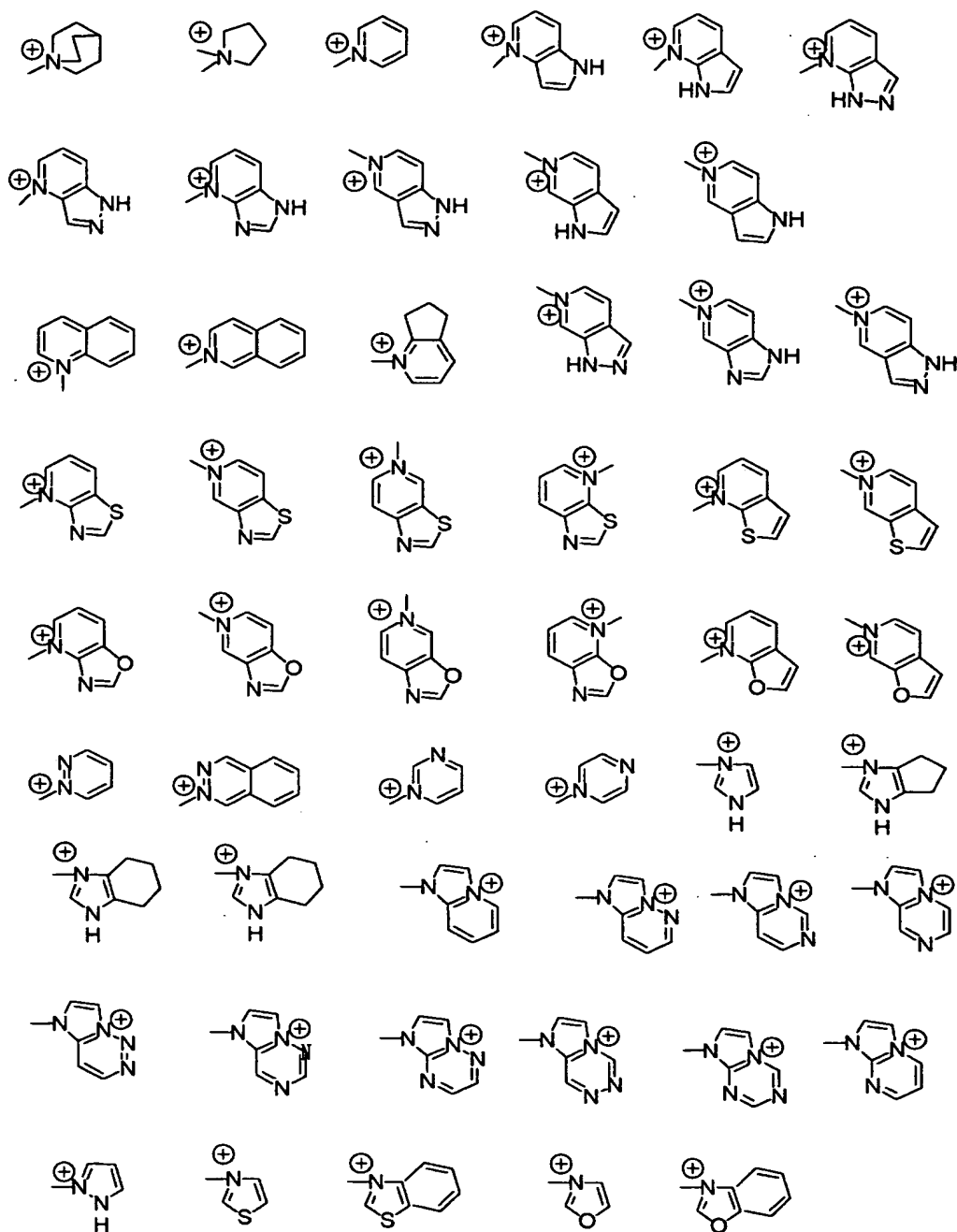
and a saturated or unsaturated, monocyclic or condensed quaternary ammonium group which contains 1 or more, preferably 1 to 4, and more preferably 1 to 3 of N
15 atoms, and optionally substituted with 1 to 4, and preferably 1 to 2 substituents. The heterocycle may further contain 1 or more of O and/or S.

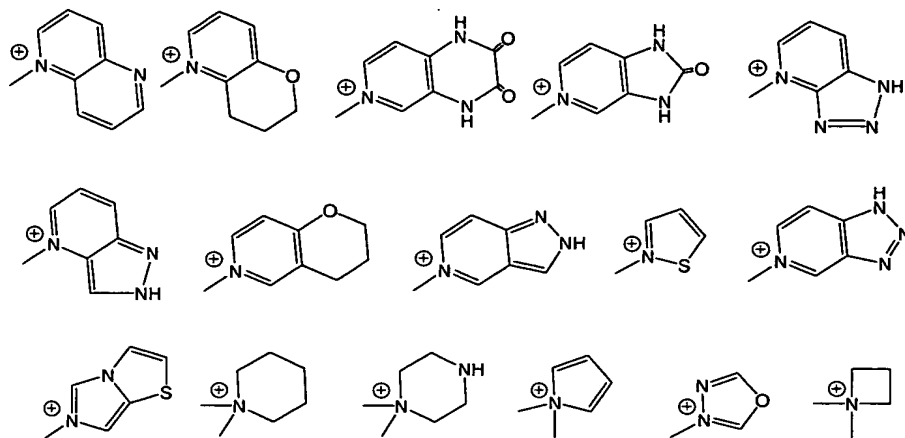
The heterocycle is preferably a 5- to 10-, preferably 5- to 6-membered cycle.

The saturated N-containing heterocycle includes pyrrolidine, pyrazolidine, thiazolidine, oxazolidine, imidazolidine, piperidine, piperazine, morpholine,
20 thiomorpholine, and a condensed ring containing the same.

The unsaturated N-containing heterocycle includes a monocycle (e.g., : pyrrole, pyrazole, imidazole, oxazole, isooxazole, thiazole, isothiazole, pyridine, pyridazine, pyrimidine, pyrazine, triazine, triazole), and a condensed bicycle containing the monocycle (e.g., indole, indolizine, benzimidazole, benzpyrazole, indolizine, quinoline,
25 isoquinoline, naphthylizine, phthalazine, quinazoline, quinuclidine, benzoisooxazole, benzpyrazole, benzoxazole, benzoxadiazole, benzisothiazole, benzothiazole, benzotriazole, purine, indoline, pyrazoloimidazole, pyridazineimidazole, thiazoloimidazole, tetrahydropyranopyridine, oxazolo[4,5-c]pyridine, oxazolo[5,4-c]pyridine, 1H-pyrrolo[3,2-b]pyridine, 1H-pyrrolo[2,3-b]pyridine, 1H-pyrrolo[3,2-c]pyridine, 1H-pyrrolo[2,3-c]pyridine, 1H-pyrazolo[4,3-b]pyridine, 1H-pyrazolo[3,4-b]pyridine, 1H-imidazo[4,5-c]pyridine, 1H-imidazo[4,5-b]pyridine, thiazolo[4,5-c]pyridine, thiazolo[5,4-b]pyridine, 1,4-dihydro-pyrido[3,4-b] pyrazine, 1,3-dihydro-imidazo[4,5-c]pyridine, triazolopyridine).

In detail, Z^+ includes optionally substituted heterocyclic groups shown below.





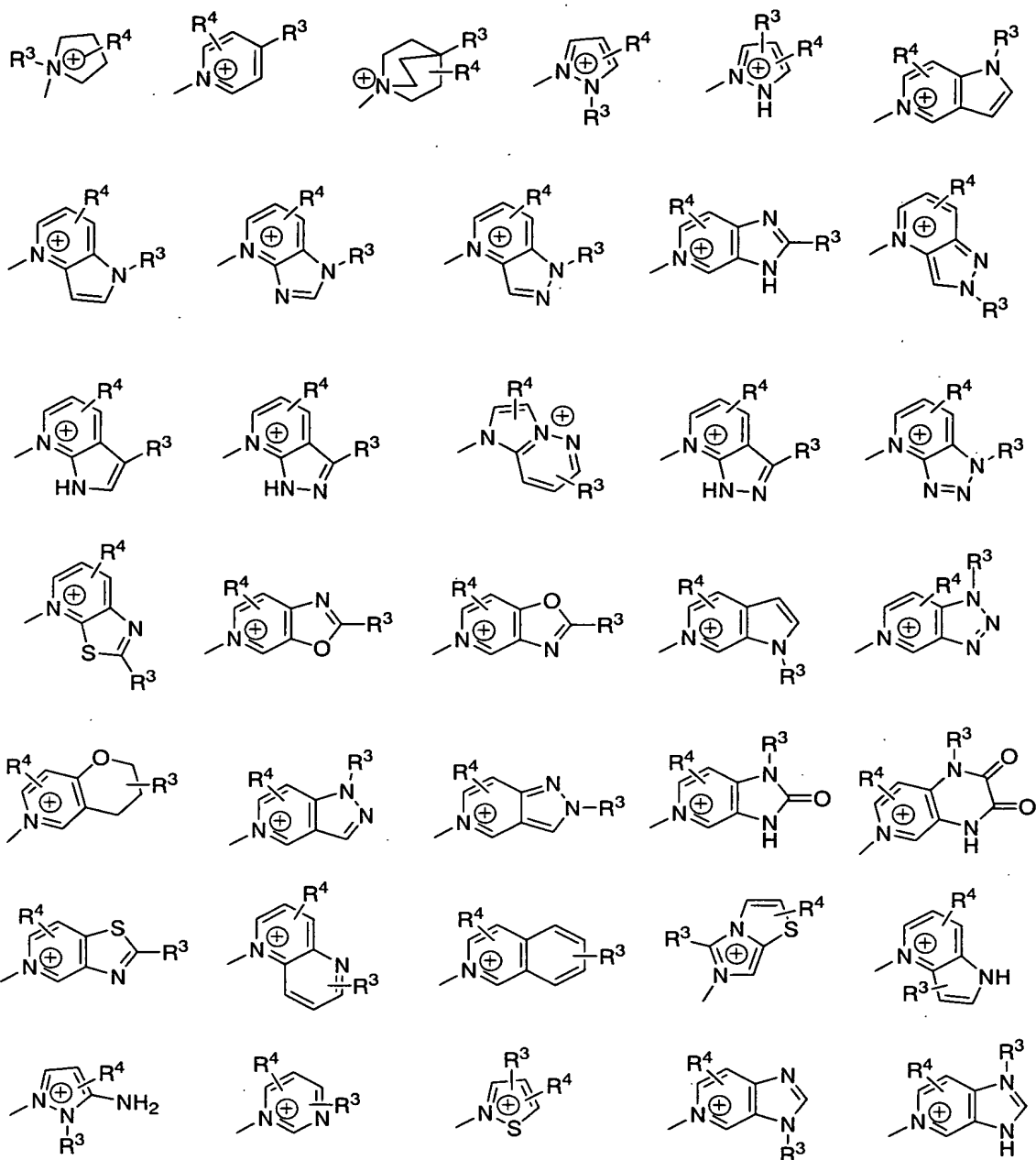
When the above heterocyclic group has a substituent(s), the substituents include 1 or more, preferably 1 to 4, more preferably 1 to 3, and most preferably 1 to 2, same or different substituent selected from the group consisting of lower alkyl (e.g., methyl, ethyl, n-butyl), optionally substituted lower alkyl (substituent: amino, lower alkylamino (e.g., -NHCH₃), optionally substituted lower alkylamino (e.g., -NHCH₂CH₂OH), optionally substituted heterocyclic group (e.g., 2-pyrrolidinyl, 3-pyrrolidinyl, 5-(3-hydroxypyrrolidinyl)), hydroxy, cycloalkyl, carboxy, lower alkoxy (e.g., methoxy), -OCOCH₃, -OCONH₂, -OCONHOCH₃, -OCONHOH, -OCONHCH₃, -OCON(CH₃)₂, -OCONHN(CH₃)₂, -ONHCOOCH₃, -CONH₂, -CONHOCH₃, -CONHOH, lower alkoxycarbonylamino (e.g., -NHCOOCH₃), lower alkylcarbonylamino (e.g., -NHCOCH₃), -NHCONH₂, -NHSO₂NH₂, -NHCHO, -N(CH₃)C=NH(NH₂), halogen, oxo); optionally substituted amino (substituent: lower alkyl (e.g., methyl, ethyl, propyl), amino lower alkyl (e.g., -CH₂CH₂NH₂, -CH₂CH(NH₂)CH₃, -CH₂CH₂CH₂NH₂), lower alkylamino(lower)alkyl (e.g., -CH₂CH₂NHCH₃, -CH₂CH₂CH₂NHCH₃), optionally substituted heterocyclic group (e.g., 3-pyrrolidinyl, 4-piperidinyl, 2-thiazolyl, 5-(1-(2-hydroxyethyl)pyrazole), 5-(1-(2-aminoethyl)pyrazole)), lower alkyl substituted with an optionally substituted heterocyclic group (e.g., (2-pyrrolidinyl)methyl, 2-(5-amino-1-(pyrazolyl)ethyl)), guanidino lower alkyl (e.g., -CH₂CH₂NHC=NH(NH₂)), hydroxy(lower)alkyl (e.g., -CH₂CH₂OH, -CH₂CH₂CH₂OH), hydroxy(lower)alkylamino(lower)alkyl (e.g., -CH₂CH₂NHCH₂CH₂OH, amino(lower)alkyloxy (e.g., -OCH₂CH₂NH₂), lower alkylamino(lower)alkyloxy (e.g., -OCH₂CH₂NHCH₃, -OCH₂CH₂CH₂NHCH₃), -CHO, =CHN(CH₃)₂, -NHCHO, optionally substituted carbamoyl (e.g., -CONH₂, -CONHCH₂CH₂NHCH₃, -CONHCH₂CH₂NHC=NH(NH₂)), -COOCH₂CH₃, -CH₂COOH, acyl (e.g., acetyl), aminoacyl (e.g., -COCH₂CH(CH₃)NH₂); optionally substituted carbamoyl

(substituent:methyl, ethyl, -NHCHO); lower alkylene (e.g., -CH₂CH₂-, -CH₂CH₂CH₂-); optionally substituted lower alkenyl (e.g., -CH₂CH=CH₂); optionally substituted cycloalkyl (e.g., cyclopropyl); hydroxy; nitro; cyano; aldehyde; optionally substituted alkyloxy (e.g., -OCH₃, -OCH₂CH₃, -OCH₂CH₂NHCH₃, -OCH₂CH₂CH₂NHCH₃); lower
5 alkylthio (e.g., -SCH₃); lower alkoxy carbonyl (e.g., -COOCH₂CH₃); halogen (e.g., F, Cl, Br), and optionally substituted heterocyclic group.

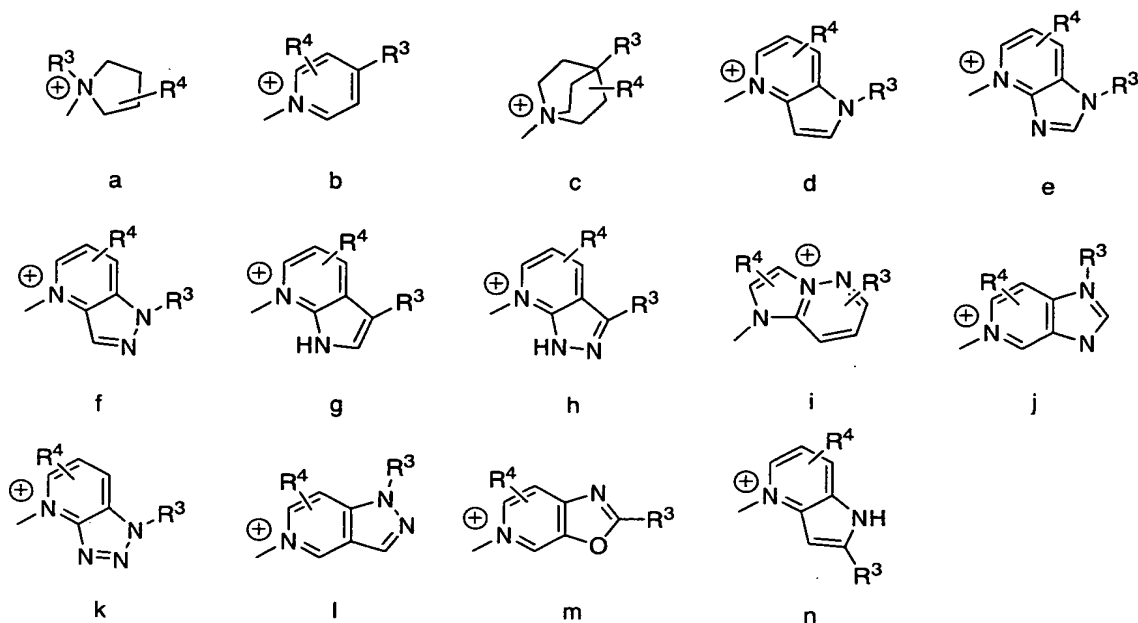
The optionally substituted heterocyclic group includes the above-mentioned Z and the bonding position is optional. Preferred is an N-containing saturated 4- to 6-
10 membered ring, for example, azetidiny (e.g., 3-azetidiny), pyrrolidinyl (e.g., 3-pyrrolidinyl), piperidinyl (e.g., 4-piperidinyl, 1-(4-aminopiperidinyl), piperadiny (e.g., 1-piperadiny, 1-(3-methylpiperadiny), pyrrolyl (e.g., 3-pyrrolyl, 4-(2-carbamoyl pyrrolyl)), pyrazolyl (e.g., 1-pyrazolyl, 4-pyrazolyl), oxadiazolyl (e.g., 2-oxadiazolyl), triazolyl (e.g., 1-triazolyl).

15 The above "lower" preferably means C1 to C6, and more preferably C1 to C3. The substituents on the heterocyclic group include preferably optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted amino and optionally substituted heterocyclic group, including the following R³ and R⁴, "-R", and "-NHR".

20 Z⁺ is preferably the following heterocyclic group.

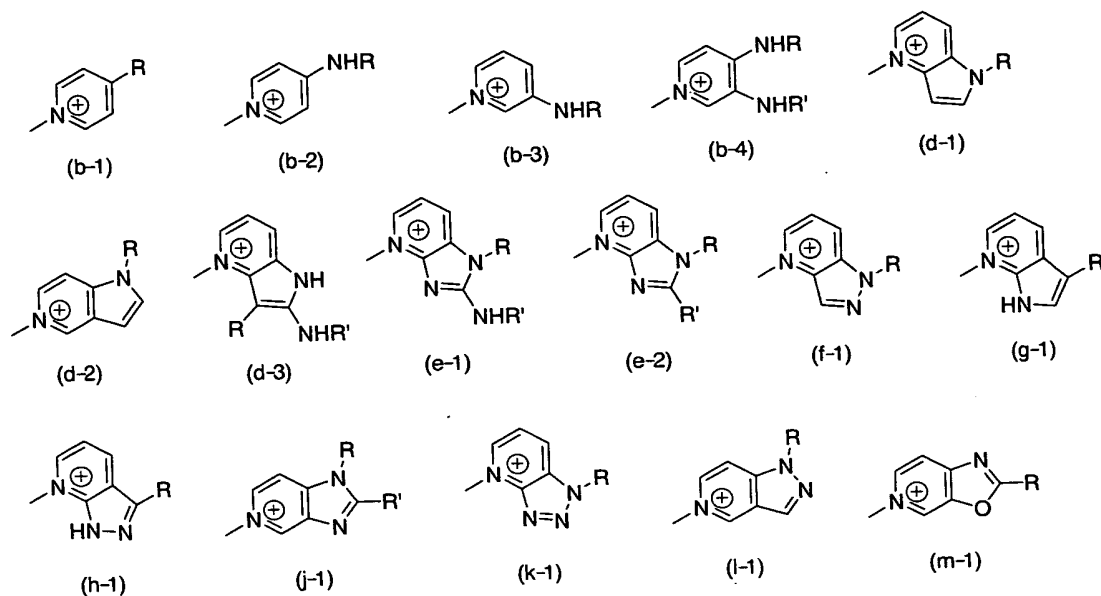


Z⁺ is more preferably the following heterocyclic group, and more preferably a group shown by b, d, e or n.



R^3 and R^4 are each selected from the substituents of the above-mentioned
 5 heterocycle, and preferred is hydrogen, the above-mentioned optionally substituted
 lower alkyl, optionally substituted lower alkenyl, optionally substituted amino or
 optionally substituted heterocyclic group, including the following “-R”, “-R”, “-NHR”, “-
 NHR”. R^3 and R^4 are each can locate at any substitutable position.

Z^+ is preferably the following heterocyclic group, and more preferably b-1, b-2, d-1,
 10 d-3, or e-1.



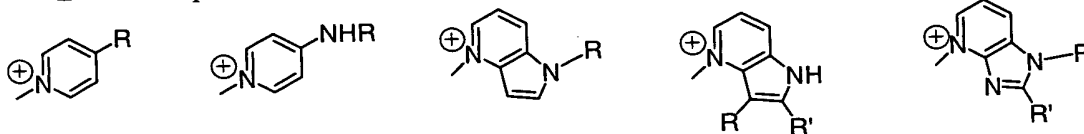
Each R and R' can be selected from the substituents of the above-mentioned heterocycle, and preferred is independently hydrogen, optionally substituted lower alkyl, optionally substituted amino, or optionally substituted heterocyclic group. More preferred is hydrogen, lower alkyl, lower alkenyl, amino lower alkyl, aminohydroxy (lower)alkyl, lower alkylamino(lower)alkyl, hydroxy(lower)alkyl, acyloxyamino(lower)alkyl, acylamino(lower)alkyl, sulfonylamino(lower)alkyl, carbamoyloxy(lower)alkyl, lower alkylhydrazonoxy(lower)alkyl, carbamoylamino(lower)alkyl, alkoxycarbonylaminoxy(lower)alkyl, lower alkoxy(lower) alkyl, carbamoyl(lower)alkyl, optionally substituted cycloalkyl, lower alkyl substituted with an optionally substituted heterocyclic group, carboxy(lower)alkyl, lower alkoxycarbonylamino(lower)alkyl, halogeno(lower)alkyl, lower alkylamino, amino (lower)alkylamino, lower alkylamino(lower)alkylamino, lower alkylamino, hydroxy(lower)alkylamino(lower)alkylamino, carbamoyloxy(lower)alkylamino, guanidino(lower)alkylamino, optionally substituted carbamoyl, optionally substituted alkyloxy, optionally substituted carbonylamino, amino substituted with an optionally substituted heterocyclic group, amino(lower)alkyloxy, or optionally substituted heterocyclic group.

R is preferably hydrogen, methyl, ethyl, cyclopropyl, $-\text{CH}_2\text{CH}_2\text{NH}_2$, $-\text{CH}_2\text{CH}_2\text{NHCH}_3$, $-\text{CH}_2\text{CH}_2\text{CH}_2\text{NHCH}_3$, $-\text{CH}_2\text{CH}_2\text{NHCH}_2\text{CH}_2\text{OH}$, $-\text{CH}_2\text{CH}_2\text{CH}_2\text{NHCH}_2\text{CH}_2\text{OH}$, $-\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}_2$, $-\text{CH}_2\text{CH}(\text{NH}_2)\text{CH}_3$, $-\text{CH}_2\text{CH}_2\text{CH}(\text{NH}_2)\text{CH}_2\text{OH}$, $-\text{CH}_2\text{CH}_2\text{CH}(\text{NH}_2)\text{CH}_2\text{OCOCH}_3$, $-\text{CH}_2\text{CH}(\text{NHCH}_3)\text{CH}_3$, $-\text{CH}_2\text{CH}_2\text{OH}$, $-\text{CH}_2\text{CH}_2\text{OCONH}_2$, $-\text{CH}_2\text{CH}_2\text{OCONHOCH}_3$.

$\text{CH}_2\text{CH}_2\text{OCONHCH}_3$, $-\text{CH}_2\text{CH}_2\text{OCON}(\text{CH}_3)_2$, $-\text{CH}_2\text{CH}_2\text{OCONHN}(\text{CH}_3)_2$,
 $\text{CH}_2\text{CH}_2\text{OCONHOH}$, $-\text{CH}_2\text{CH}_2\text{CH}_2\text{OCONH}_2$, $-\text{CH}_2\text{CH}_2\text{ONHCOOCH}_3$,
 $\text{CH}_2\text{CH}_2\text{NHCOOH}$, $-\text{CH}_2\text{CONH}_2$, $-\text{CH}_2\text{CONHOCH}_3$, $-\text{CH}_2\text{CONHOH}$, $-\text{CH}_2\text{COOH}$,
 $\text{CH}_2\text{CH}_2\text{NHCOCH}_3$, $-\text{CH}_2\text{CH}_2\text{NHCONH}_2$, $-\text{CH}_2\text{CH}_2\text{NHSO}_2\text{NH}_2$, $-\text{CH}_2\text{CH}_2\text{NHCOOCH}_3$,
5 $-\text{CH}_2\text{CH}_2\text{NHC}(\text{NH}_2)=\text{NH}$, $-\text{CH}_2\text{CH}_2\text{CH}_2\text{N}(\text{CH}_3)\text{C}(\text{NH}_2)=\text{NH}$, NH_2 , $-\text{NHCH}_2\text{CH}_2\text{NH}_2$,
 $\text{NHCH}_2\text{CH}_2\text{NHCH}_3$, $-\text{NH}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{NHCH}_3$, $-\text{N}(\text{CHO})\text{CH}_2\text{CH}_2\text{NHCH}_3$,
 $\text{NHCOCH}_2\text{CH}(\text{NH}_2)\text{CH}_3$, $-\text{CONHCH}_2\text{CH}_2\text{NHCH}_3$, $-\text{CONHCH}_2\text{CH}_2\text{NHC}(\text{NH}_2)=\text{NH}$,
 $\text{OCH}_2\text{CH}_2\text{NHCH}_3$, 3-azethidiny, 3-pyrrolidinylamino, 3-pyrrolidinyl, 1-pyrazolyl, 5-(1-(2-hydroxyethyl)pyrazolyl, 5-(1-(2-aminoethyl)pyrazolyl), 2-(1-(5-aminopyrazolyl))ethyl,
10 4-pyrazolyl, 3-pyrazolyl, 4-(2-carbamoylpyrolyl), 2-pyrrolidinylmethyl, 3-pyrrolidinylmethyl, 5-(3-hydroxypyrrolidinyl)methyl, 2-thiazolyl, 2-oxadiazolyl, 1-triazolyl, 1-(3-methylpiperadiny), 1-(4-aminopiperidinyl), or 4-piperidinyl.

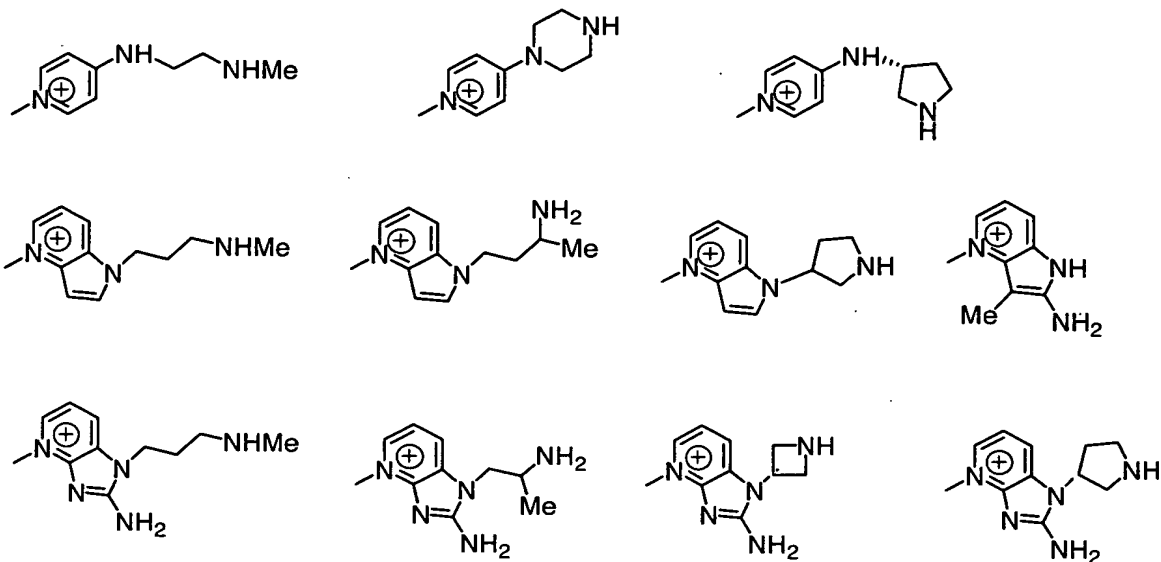
R' is preferably hydrogen or optionally substituted amino. R' is preferably hydrogen, $-\text{NH}_2$, $-\text{NHCH}_3$, $-\text{N}(\text{CH}_3)_2$, $-\text{N}=\text{CHN}(\text{CH}_3)_2$, $-\text{N}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{NH}_2$,
 15 $\text{NHCH}_2\text{CH}_2\text{NHCH}_3$, $-\text{NHCOOCH}_2\text{CH}_3$, $-\text{NHOCH}_3$, or $-\text{NHCH}_2\text{COOH}$.

Z⁺ is more preferably the following group.



20 (wherein, each R is independently hydrogen, lower alkyl, amino lower alkyl, lower alkylamino(lower)alkyl, amino substituted with an optionally substituted heterocyclic group, or optionally substituted heterocyclic group ; R' is amino)

Z⁺ is most preferably the following group.

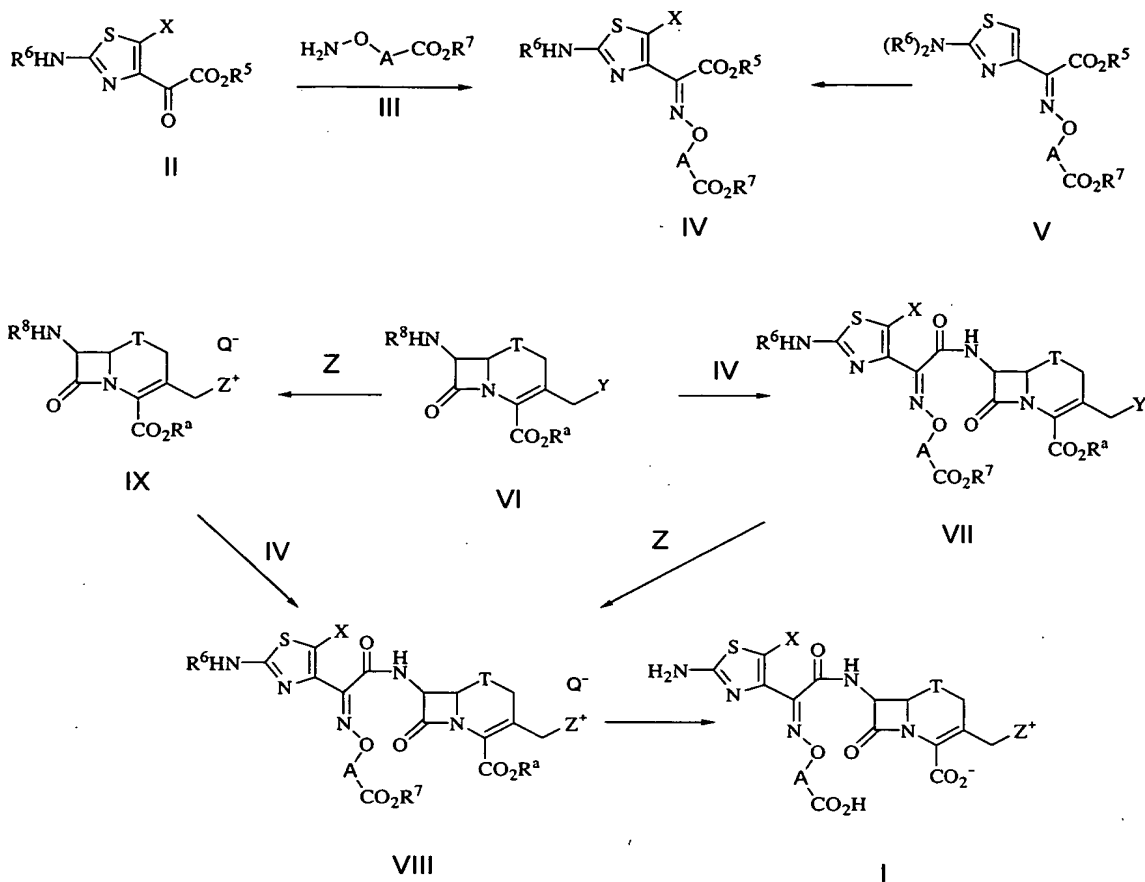


Compound (I) preferably includes the following compounds.

- 5 (a) a compound wherein T is S ; X is halogen or lower alkyl ; A is a divalent group shown in any of the above (5) to (9) ; Z⁺ is a heterocyclic group shown in any of the above-mentioned (10) to (14).
- (b) a compound wherein T is S ; X is halogen or lower alkyl ; A is a divalent group shown in any of the above (8) ; Z⁺ is a heterocyclic group shown in the above-mentioned
- 10 (12). Preferably, X is halogen and Z⁺ is the above-mentioned (b-1), (b-2), (d-1), (d-3), (e-1), or (e-2).
- (c) a compound wherein T is S ; X is halogen ; A is a divalent group shown in the above
- (9) ; Z⁺ is a heterocyclic group shown in the above-mentioned (13) or (14).

- 15 Preferred embodiments include compounds of Examples 1, 3, 4, 5, 8, 9, 18, 19, 20, 79, 98, 111, 112, 124, 128, 132, 161, 164, and 185, and more preferred are compounds of Examples 8, 9, 18, 20, 79, 98, 124, 128, 132, 161, and 164.

The representative method for preparing compound (I) is explained below.



(wherein, T is the same as defined above ; R^5 is hydrogen or carboxy-protecting group ; R^6 is hydrogen or amino-protecting group ; R^7 is hydrogen or carboxy-protecting group ; R^8 is hydrogen or amino-protecting group ; R^a is hydrogen or carboxy-protecting group ; Y is a leaving group (e.g., hydroxy, halogen (e.g., Cl, Br, I), carbamoyloxy, substituted carbamoyloxy, acyloxy, methanesulfonyloxy, toluenesulfonyloxy) ; Q^- is a counter ion such as halogen)

10 (1) Production method of compound (IV), material of 7-side chain (Method A)

Compound (II) and compound (III) are reacted to give compound (IV). In this case, preferably R^5 is hydrogen ; R^6 is amino-protecting group ; R^7 is carboxy-protecting group.

15 The amount of compound (III) is usually about 1 to 10 mol, preferably about 1 to 2 mol per compound (II) 1 mol.

Examples of reaction solvent include ether (e.g., dioxane, tetrahydrofran, diethylether, tert-butyl methyl ether, diisopropylether), ester (e.g., ethyl formate, ethyl

acetate, n-butyl acetate), halogenated hydrocarbon (e.g., dichloromethane, chloroform, carbon tetrachloride), hydrocarbon (e.g., n-hexane, benzene, toluene), alcohol (e.g., methanol, ethanol, isopropanol), amide (e.g., formamide, N,N-dimethylformamide, N,N-dimethylacetamide, N-methylpyrrolidone), ketone (e.g., acetone, methyl ethyl ketone), nitrile (e.g., MeCN, propionitrile), dimethyl sulfoxide, water. These solvents
5 can be used as single or a mixture.

The reaction temperature is usually about -20 to 100°C, preferably about 0 to 5°C.

(Method B)

10 Compound (V) is halogenated, optionally followed by deprotection, to give compound (IV). In this case, preferably R⁵ is a carboxy-protecting group in compound (V) and hydrogen in compound (IV); R⁶ is an amino-protecting group; R⁷ is a carboxy-protecting group.

Examples of halogenating agent include N-chlorosuccinimide, N-chlorophthalimide, Cl₂, N-bromosuccinimide, N-bromophthalimide, Br₂, and F₂.
15

The amount of halogenating agent is usually about 1 to 20mol, preferably about 1 to 2mol per compound (V) 1mol.

Examples of reaction solvent are the same as mentioned above.

The reaction temperature is usually about -10 to 100°C, preferably about 0 to
20 50 °C.

(2) Acylation at 7-position and 3-Side chain formation; production of compound (VII) and (VIII)

1) Acylation at 7-position

25 Compound (VI) and compound (IV) are reacted to give compound (VII). Preferably, R^a is a carboxy-protecting group; R⁵ is hydrogen; R⁶ is an amino-protecting group; R⁷ is a carboxy-protecting group; R⁸ is hydrogen.

The amount of compound (IV) is usually about 1 to 5 mol, preferably about 1 to 2mol per compound (VI) 1mol.

30 Examples of solvents used in the reaction include ethers (e.g., dioxane, THF, diethylether, tert-butylmethylether, and diisopropylether), esters (e.g., ethyl formate, ethyl acetate, and n-butyl acetate), halogenated hydrocarbons (e.g., dichloromethane, chloroform, and carbon tetrachloride), hydrocarbons (e.g., n-hexane, benzene, and toluene), amides (e.g., formamide, N,N-dimethylformamide (DMF), N,N-dimethylacetoamide, and N-methylpyrrolidone), ketones (e.g., acetone and
35

methylethylketone), nitriles (e.g., MeCN and propionitriles), dimethylsulfoxide, and water.

The reaction temperature is usually about -40 to 100°C, preferably about 0 to 30°C. Compound (VI, VII, VIII, T=SO) can be prepared by oxidating compound (VI, VII, VIII, T=S). Preferably, compound (VII, T=SO) can be prepared by oxidating compound (VII, T=S).

Examples of oxidating agent include m-chloroperoxybenzoic acid (m-CPBA), hydrogen peroxid, and peracetic acid.

Compound (VI) can be prepared according to the method described in JP Patent publication (Kokai) S-60-231684, JP Patent publication (Kokai) S-62-149682 or the like.

The above amidation can be conducted after conversion of the carboxyl moiety into a reactive derivative. Examples of the reactive derivative include inorganic base salts, organic base salts, acid halides, acid azides, acid anhydrides, mixed acid anhydride, active amide, active ester, active thioester. The inorganic base includes alkaline metals (e.g., Na and K) and alkaline earth metals (e.g., Ca and Mg); The organic base includes trimethylamine, triethylamine, tert-butyldimethylamine, dibenzylmethylamine and benzyldimethylamine; the acid halide includes acid chloride and acid bromide; the mixed acid anhydride includes mixed monoalkylcarboxylic acid anhydride, mixed aliphatic carboxylic acid anhydride, aromatic carboxylic acid anhydride, organic sulfonic acid anhydride, the active amide includes amide formed with heterocyclic compound containing N atom, for example. Examples of the active ester include organic phosphate esters (e.g., diethoxy phosphate ester and diphenoxy phosphate ester), p-nitrophenyl ester, 2,4-dinitrophenyl ester, cyanomethyl ester, and the active thioester includes esters formed with aromatic heterocyclicthio compound (e.g., 2-pyridylthio ester).

The above reaction may be carried out using an appropriate condensing agent, if necessary. Examples of the condensing agent include e.g., 1-dimethylaminopropyl-3-ethylcarbodiimide · hydrochloride (WSCD · HCl), N,N'-dicyclohexylcarbodiimide, N,N'-carbonyldiimidazole, N,N'-thiocarbonyldiimidazole, N-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline, phosphorus oxychloride, alkoxyacetylene, 2-chloropyridiniummethyl iodine, and 2-fluoropyridiniummethyl iodine, trifluoroacetic acid anhydride.

2) 3-Side chain formation

Compound (VII) and Z (optionally substituted N-containing heterocycle) is reacted

to give compound (VIII). Preferably, R^6 is an amino-protecting group ; R^7 is a carboxy-protecting group ; R^a is a carboxy-protecting group. Compound (VIII) may have a functional group as a substituent on Z, which can be protected.

5 The amount of Z is usually about 1 to 10 mol, preferably about 1 to 2 mol per compound (VII) 1 mol.

Examples of solvents include ethers (e.g., dioxane, THF, diethyl ether, tert-butyl methyl ether, and diisopropyl ether), esters (e.g., ethyl formate, ethyl acetate, and n-butyl acetate), halogenated hydrocarbons (e.g., dichloromethane, chloroform, and carbon tetrachloride), hydrocarbons (e.g., n-hexane, benzene, and toluene), amides (e.g.,
10 formamide, N,N-dimethylformamide (DMF), N,N-dimethylacetoamide, and N-methylpyrrolidone), ketones (e.g., acetone and methyl ethyl ketone), nitriles (e.g., MeCN and propionitrile), dimethyl sulfoxide, and water.

The reaction temperature is usually about 0 to 100°C, preferably about 0 to 50°C, and more preferably about 10 to 30°C.

15 Examples of reaction-accelerating agent include NaI.

Compound (VIII, T=S) can be prepared by reducing compound (VIII, T=SO). The reducing agent includes metals (e.g., Zn, Sn) and iodide (e.g., KI).

(3) 3-Side chain formation and Acylation at 7-position ; production of compound (IX)
20 and (VIII)

1) 3-side chain formation

Compound (VI) and Z (optionally substituted N-containing heterocycle) are reacted to give compound (IX). Preferably, R^8 is hydrogen ; R^a is a carboxy-protecting group. Compound (VIII) may have a functional group as a substituent on Z, which
25 can be protected.

The amount of Z is usually about 1 to 10 mol, preferably about 1 to 2 mol per compound (VI) 1 mol.

Examples of solvents include ethers (e.g., dioxane, THF, diethyl ether, tert-butyl methyl ether, and diisopropyl ether), esters (e.g., ethyl formate, ethyl acetate, and n-
30 butyl acetate), halogenated hydrocarbons (e.g., dichloromethane, chloroform, and carbon tetrachloride), hydrocarbons (e.g., n-hexane, benzene, and toluene), amides (e.g., formamide, N,N-dimethylformamide (DMF), N,N-dimethylacetoamide, and N-methylpyrrolidone), ketones (e.g., acetone and methyl ethyl ketone), nitriles (e.g., MeCN and propionitrile), dimethyl sulfoxide, and water.

35 The reaction temperature is usually about 0 to 100°C, preferably about 0 to 50°C,

and more preferably about 10 to 30°C.

Examples of reaction-accelerating agent include NaI.

Compound (IX, T=SO) can be prepared by oxidating compound (IX, T=S).

Examples of oxidating agent include m-chloroperoxybenzoic acid (m-CPBA),
5 hydrogen peroxid, and peracetic acid.

2) Acylation at 7-position

Compound (IX) and compound (IV) are reacted to give compound (VIII).
Preferably, R^a is a carboxy-protecting group; R⁵ is hydrogen; R⁶ is an amino-protecting
10 group; R⁷ is a carboxy-protecting group; R⁸ is hydrogen.

The amount of compound (IV) is usually about 1 to 5 mol, preferably about 1 to 2
mol per compound (IX) 1 mol.

Examples of solvents include ethers (e.g., dioxane, THF, diethyl ether, tert-
butylmethyl ether, and diisopropyl ether), esters (e.g., ethyl formate, ethyl acetate, and
15 n-butyl acetate), halogenated hydrocarbons (e.g., dichloromethane, chloroform, and
carbon tetrachloride), hydrocarbons (e.g., n-hexane, benzene, and toluene), amides (e.g.,
formamide, N,N-dimethylformamide (DMF), N,N-dimethylacetoamide, and N-
methylpyrrolidone), ketones (e.g., acetone and methyl ethyl ketone), nitriles (e.g.,
MeCN and propionitrile), dimethyl sulfoxide, and water.

20 The reaction temperature is usually about -40 to 100°C, preferably about 0 to
30°C, and more preferably about 10 to 30°C.

The above amidation can be conducted after conversion of the carboxyl moiety
into a reactive derivative or by using an appropriate condensing agent. Examples of
the reactive derivative include inorganic base salts, organic base salts, acid halides,
25 acid azides, acid anhydrides, mixed acid anhydride, active amide, active ester, active
thioester.

(4) Deprotection

Compound (VIII) can be deprotected by a method well known to a person skilled in
the art to give compound (I).

30 Examples of solvents include ethers (e.g., dioxane, THF, diethyl ether, tert-
butylmethyl ether, and diisopropyl ether), esters (e.g., ethyl formate, ethyl acetate, and
n-butyl acetate), halogenated hydrocarbons (e.g., dichloromethane, chloroform, and
carbon tetrachloride), hydrocarbons (e.g., n-hexane, benzene, and toluene), amides (e.g.,
formamide, N,N-dimethylformamide (DMF), N,N-dimethylacetoamide, and N-
35 methylpyrrolidone), ketones (e.g., acetone and methyl ethyl ketone), nitriles (e.g.,

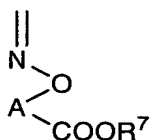
MeCN and propionitrile), dimethyl sulfoxide, and water.

The reaction temperature is usually about -30 to 100°C, preferably about 0 to 50°C, and more preferably about 0 to 10°C.

Examples of catalyst include Lewis acid (e.g., AlCl₃, SnCl₄, TiCl₄) and protonic acid
5 (e.g., HCl, H₂SO₄, HClO₄, HCOOH, phenol).

Thus obtained compound (I) can further be chemically modified to give the other compound (I), ester, amino-protected compound wherein the amino bonds to a thiazole ring at the 7-position, or pharmaceutically acceptable salt or solvate thereof.

Ester of compound (I) preferably includes esters which is formed at carboxyl
10 moiety on the 7-side chain or at the 4-position. The ester compound formed at carboxyl moiety on the 7-side chain means a compound having an ester structure of the formula:

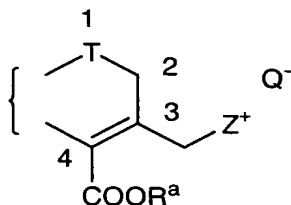


15

(R⁷ is an ester residue such as carboxy-protecting group)

The ester includes an ester which is readily metabolized in the body to carboxy.

The ester compound formed at the carboxyl moiety at the 4-position means a compound having an ester structure of the formula:



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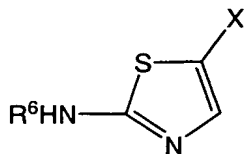
(R^a is an ester residue such as carboxy-protecting group ; Q⁻ is an counter ion such as halogen)

The ester includes an ester readily metabolized in the body to carboxy.

25

Examples of the above carboxy-protecting group include lower alkyl (e.g., methyl, ethyl, t-butyl), (substituted)aralkyl (e.g., benzyl, benzhydryl, p-methoxybenzyl, p-nitrobenzyl), silyl group (e.g., t-butyldimethylsilyl, diphenyl t-butylysilyl).

The amino-protected compound (I) wherein the amino bonds to a thiazole ring at the 7-position means a compound wherein the thiazole ring is of the formula :



(R⁶ is an amino-protecting group) The amino-protecting group includes that which is readily metabolized in the body to amino. The above amino-protecting group includes
 5 lower alkoxycarbonyl (e.g., t-butoxycarbonyl, benzyloxycarbonyl, p-nitrobenzyloxy carbonyl), (substituted) aralkanoyl (e.g., p-nitrobenzoyl), acyl (e.g., formyl, chloro acetyl).

Examples of the pharmaceutically acceptable salt of compound (I) include salts formed with inorganic bases, ammonia, organic bases, inorganic acids, organic acids,
 10 basic amino acids, halogen ions or the like, and inner salts. Examples of the inorganic base include alkali metal (e.g., Na and K) and alkaline earth metal (e.g., Mg).

Examples of the organic base include procaine, 2-phenylethylbenzylamine, dibenzylethylenediamine, ethanolamine, diethanolamine, tris(hydroxymethyl)aminomethane, polyhydroxyalkylamine, and N-methyl
 15 glucosamine. Examples of the inorganic acid include hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, and phosphoric acid. Examples of the organic acid include p-toluene sulfonic acid, methanesulfonic acid, formic acid, trifluoroacetic acid and maleic acid. Examples of the basic amino acid include lysine, arginine, ornithine and histidine. Examples of solvate of compound (I) include water and alcohol.

20

The present invention further provides the above-mentioned compound (I-A). The definition of each group in compound (I-A) and production method thereof are in accordance with those for the above-mentioned compound (I).

25 Further, the present invention provides the above-mentioned compound (IV), (VII) and (IX). These compounds are useful as intermediates of compound (I). In particular, compound (IV) is an important intermediate for the exhibition of antibacterial activity of compound (I).

In compound (IV), X is preferably halogen or lower alkyl and more preferably
 30 halogen (e.g., Cl, Br).

The invention compounds with a broad antibacterial spectrum are useful for the prevention or treatment of various diseases caused by enteropathogenic bacteria of

mammals, including respiratory tract infection, urinary tract infection, respiratory tract infection, septicemia, nephritis, cholecystitis, oral infection, endocarditis, pneumonia, bone meningitis, otitis media, enteritis, empyema, wound infection, and opportunistic infection.

5

The invention compound exhibits a potent antibacterial activity, preferably against gram-negative bacteria including *Pseudomonas*, *E. coli*, and *Haemophilus influenzae*. In particular, the compound is extremely stable against β -lactamase, esp., C-class β -lactamase, produced by cephem-resistant *Pseudomonas*, thus being
10 efficacious against the *Pseudomonas*. Accordingly, the invention compound can bring an excellent clinical effect even by single use without a β -lactamase inhibitor. Further, the invention compound possesses an antibacterial activity against gram-positive bacteria including methicillin-resistant *Staphylococcus aureus* (MRSA) and penicillin-resistant *Staphylococcus aureus* (PRSE). Moreover, it has some excellent
15 characteristics in the pharmacokinetics, such as blood concentration, continuous effect, and transition into tissues. In another embodiment, the invention compound has a high water solubility and particularly suitable for an injection agent.

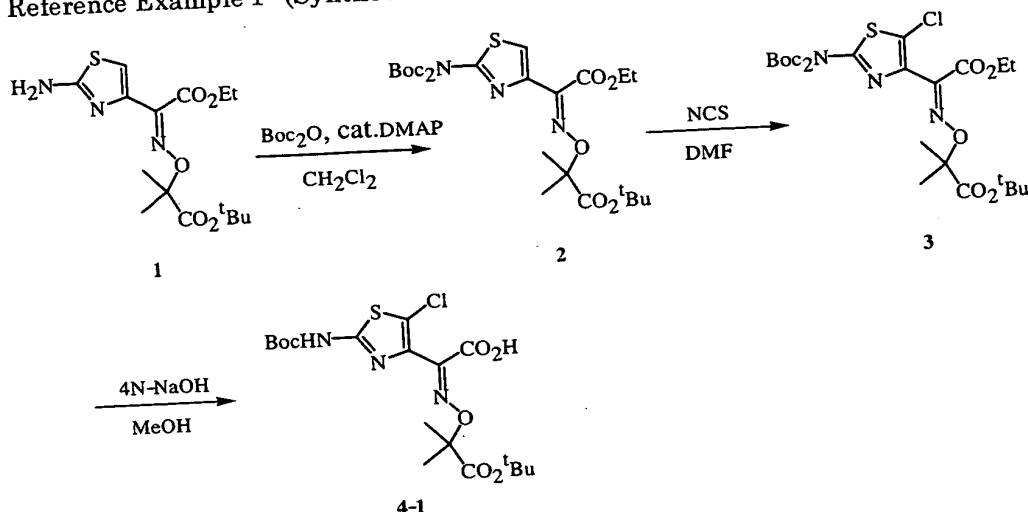
Compound (I) or (I-A) can be administered parenterally or orally as an agent of injection, capsule, tablet or granule. Preferably, it can be administered as an injection
20 agent. The daily dose for a patient or animal is usually about 0.1 to 100 mg/kg, preferably about 0.5 to 50 mg/kg, optionally in 2 to 4 divisions. The pharmaceutically acceptable carriers used for injections include e.g., distilled water, physiologic saline, and pH adjusting agents such as bases. For preparing capsules, granules, and tables, other pharmaceutically acceptable carriers can be used, such as excipients (e.g., starch,
25 lactose, sucrose, calcium carbonate, calcium phosphate), binders (e.g., starch, Arabian gum, carboxymethyl cellulose, hydroxypropyl cellulose, crystalline cellulose), and lubricants (e.g., magnesium stearate, talc).

Reference Examples and Examples are shown below.

30 (Abbreviation)

Me : methyl ; Et : ethyl ; iPr : isopropyl ; Bu : butyl ; Ac : acetyl ; DMF : dimethylformamide ; THF : tetrahydrofuran ; DMA : dimethylacetamide ; WSCD : 1-dimethylaminopropyl-3-ethylcarbodiimide ; m-CPBA : m-chloroperoxybenzoic acid ; Boc : t-butoxycarbonyl ; PMB : p-methoxybenzyl ; BH : benzhydryl ; TBS : t-
35 butyldimethylsilyl ; Ph : phenyl

Reference Example 1 (Synthesis of 7-side chain)



(1) To a solution of compound 1 (71.4g, 200mmol) in dry CH_2Cl_2 714ml, was added at room temperature 4-dimethylaminopyridine (DMAP) 2.44g (0.1eq) and Boc_2O 95.2ml (2.1eq) was added dropwise. The reaction mixture was stirred at room temperature for 21 hr, which was poured to a saturated NH_4Cl aq. solution containing 1N-HCl 19ml, then the organic layer was separated, washed with brine, dried over anhydrous Na_2SO_4 , and concentrated in vacuum to give compound 2 (112g).

$^1\text{H-NMR}$ (CDCl_3) δ : 1.35(3H, t, $J = 6.9$ Hz), 1.43(9H, s), 1.51(6H, s), 1.53(18H, s), 4.36(2H, q, $J = 6.9$ Hz), 7.38(1H, s).

IR (KBr) cm^{-1} : 2979, 2938, 1781, 1743, 1722, 1494, 1457, 1369, 1346, 1328, 1284, 1135.

MS(ESI): 558 $^+$ ($\text{M}+\text{H}^+$).

Elemental analysis $\text{C}_{25}\text{H}_{39}\text{N}_3\text{O}_9\text{S}$.

Calc. : C, 53.84 ; H, 7.05 ; N, 7.54 ; S, 5.75 (%).

Found : C, 53.70 ; H, 6.91 ; N, 7.49 ; S, 5.81 (%).

(2) To a solution of compound 2 101g (181mmol) in DMF 400 ml, was added at room temperature N-chlorosuccinimide (NCS) 9.65g (0.4eq) and the mixture was stirred at room temperature for 3 hr. NCS 9.65g (0.4eq) was added thereto and the mixture was stirred at room temperature for 2 hr, then NCS 9.65g (0.4eq) was further added followed by 4 hr stirring at room temperature. The mixture was allowed to stand at 4 $^{\circ}\text{C}$ overnight, which was poured to 1000ml water containing Na_2SO_4 30g, followed by extraction with AcOEt (500ml \times 2). The obtained organic layer was washed with brine, dried over anhydrous Na_2SO_4 , and concentrated in vacuum. Purification with silica gel column chromatography, followed by

concentration in vacuum, gave compound 3 (104g).

$^1\text{H-NMR}$ (CDCl_3) δ : 1.34(3H, t, $J = 6.9$ Hz), 1.44(9H, s), 1.52(6H, s), 1.53(18H, s), 4.33(2H, q, $J = 6.9$ Hz).

IR (KBr) cm^{-1} : 2979, 2938, 1781, 1743, 1722, 1494, 1457, 1369, 1346, 1328, 1284, 1135.

5 MS(ESI): 614 $^+$ ($\text{M} + \text{Na}^+$).

Elemental analysis $\text{C}_{25}\text{H}_{38}\text{ClN}_3\text{O}_9\text{S}$.

Calc. : C, 50.71 ; H, 6.47 ; N, 7.10 ; S, 5.42 ; Cl, 5.99 (%).

Found : C, 50.57 ; H, 6.40 ; N, 7.01 ; S, 5.13 ; Cl, 5.93(%).

(3) To a solution of compound 3 83.2g (140mmol) in MeOH 1600 ml, 8N-NaOH
10 175ml was added dropwise under ice-cooling. The mixture was stirred under ice-cooling for 0.5 hr and further stirred at room temperature for 5.5 hr. 5N-HCl 210ml was added dropwise (the pH of the reaction solution is 5.3) thereto and the mixture was allowed to stand overnight at room temperature. The mixture was concentrated under reduced pressure to remove MeOH, resulting in precipitation of white
15 precipitates, followed by adding water 1000ml and filtration. The obtained white solid was washed with ice water and dried under reduced pressure to give compound 4-1 60.9g.

$^1\text{H-NMR}$ (CDCl_3) δ : 1.46(9H, s), 1.52(9H, s), 1.58(6H, s), 5.20-6.20(2H, brs).

IR (KBr) cm^{-1} : 3426, 3220, 3081, 2981, 2937, 1720, 1556, 1455, 1394, 1369, 1249, 1155.

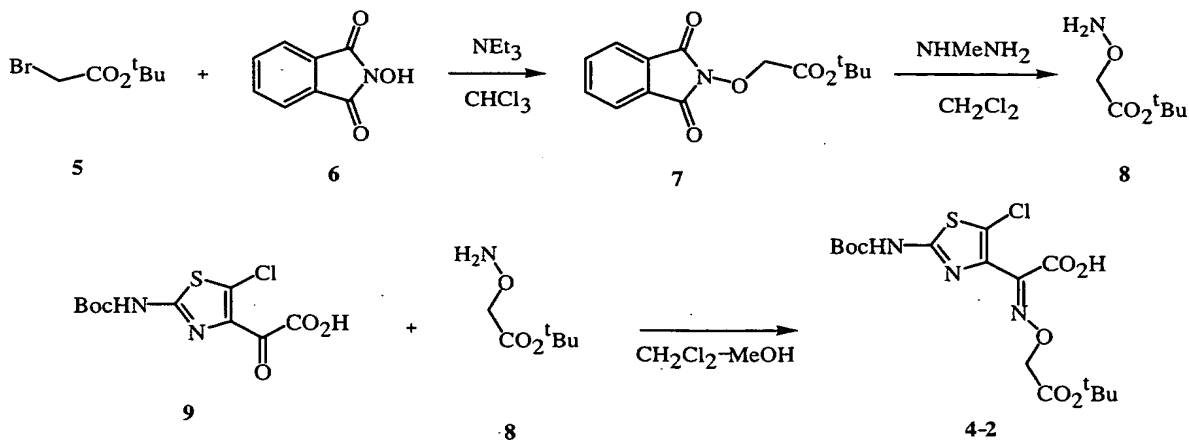
20 MS(ESI): 464 $^+$ ($\text{M} + \text{H}^+$).

Elemental analysis $\text{C}_{18}\text{H}_{26}\text{ClN}_3\text{O}_7\text{S} \cdot 0.6 \text{H}_2\text{O}$.

Calc. : C, 45.54 ; H, 5.77 ; N, 8.85 ; S, 6.75 ; Cl, 7.47 (%).

Found : C, 45.38 ; H, 5.59 ; N, 8.82 ; S, 6.67 ; Cl, 7.75(%).

25 Reference Example 2 (Synthesis of 7-side chain)



(1) To a solution of compound 5 (8.8ml, 60 mmol) and compound 6 (6.52g 40mmol) in dry CHCl_3 180ml, was added dropwise triethylamine 6.12ml under ice-cooling, and the mixture was stirred at room temperature for 3 days. After adding triethylamine 3.0ml, the mixture was further stirred at room temperature for 1 day, which was
5 poured to a saturated NaHCO_3 aq. solution, followed by extraction with CHCl_3 . The obtained organic layer was washed with a saturated NH_4Cl aq. solution, dried over anhydrous MgSO_4 , and concentrated under reduced pressure to give compound 7 (10.5g).

$^1\text{H-NMR}$ (CDCl_3) δ : 1.49(9H, s), 4.71(2H, s), 7.70-7.90(4H, m).

10 IR (KBr) cm^{-1} : 2980, 2939, 1788, 1745, 1730, 1465, 1441, 1374, 1247, 1186, 1160, 1137, 1043.

MS(ESI):300 $^+$ (M+Na $^+$).

Elemental analysis $\text{C}_{14}\text{H}_{15}\text{NO}_5 \cdot 0.2 \text{H}_2\text{O}$.

Calc. : C,59.87 ; H,5.53 ; N,4.99 (%).

15 Found : C,60.04 ; H,5.55 ; N,5.13 (%).

(2) To a solution of compound 7 (1.67g 6mmol) in dry CH_2Cl_2 16ml, was added methyl hydrazine 0.32ml under ice-cooling and the mixture was stirred for 15 min. The obtained white precipitations were filtered off to give compound 8 in the filtrate.

MeOH 6ml was added thereto under ice-cooling, and compound 9 (1.53g 5mmol) was
20 added thereto. After stirring under ice-cooling for 10 min, the mixture was further stirred at room temperature for 2.5 hr and under reflux for 1 hr, then allowed to stand at room temperature for 3 days. The obtained precipitation was filtered and washed with water to give compound 4-2 (1.36g).

25 $^1\text{H-NMR}$ (d_6 -DMSO) δ : 1.42(9H, s), 1.46(9H, s), 4.36(2H, s), 6.0-9.0(1H, brs), 11.9(1H, brs).

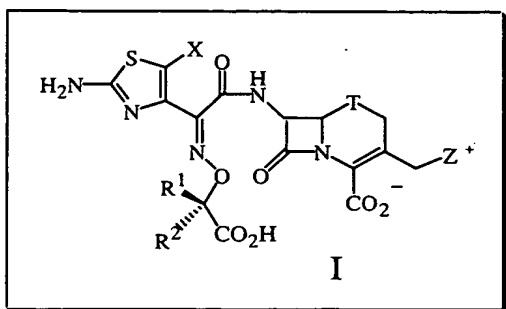
IR (KBr) cm^{-1} : 3429, 3136, 2982, 2936, 1739, 1715, 1626, 1557, 1458, 1392, 1381, 1370, 1249, 1157.

MS(FAB):434 (M-H $^-$).

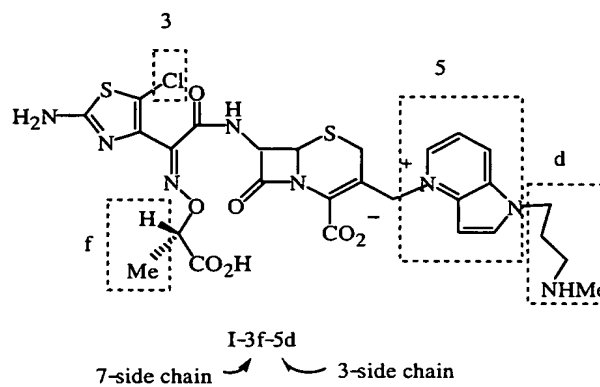
HR-MS(FAB): calcd for $\text{C}_{16}\text{H}_{21}\text{Cl}_1\text{N}_3\text{O}_7\text{S}$ 434.0789 found 434.0782.

30

The relation of substituent, compound No and structure of Example compounds are exemplified below.



Example of compound No

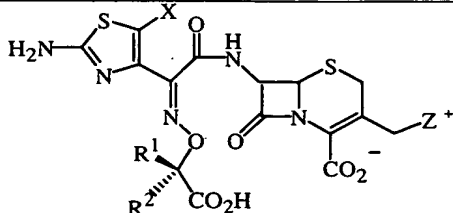


| 7-side chain | | |
|--------------|---------------------------------------|--------------------|
| X | R1 | R2 |
| 1: H | a: H | H |
| 2: Me | b: =CH ₂ | |
| 3: Cl | c: -(CH ₂) ₂ - | |
| 4: Br | d: Me | Me |
| | e: Me | H |
| | f: H | Me |
| | g: Et | H |
| | h: H | Et |
| | i: iPr | H |
| | j: H | iPr |
| | k: CH ₂ OH | H |
| | l: H | CH ₂ OH |

| 3-side chain | |
|--------------|---|
| | Z |
| 1 | |
| 2 | |
| 3 | |
| 4 | |
| 5 | |
| 6 | |
| 7 | |

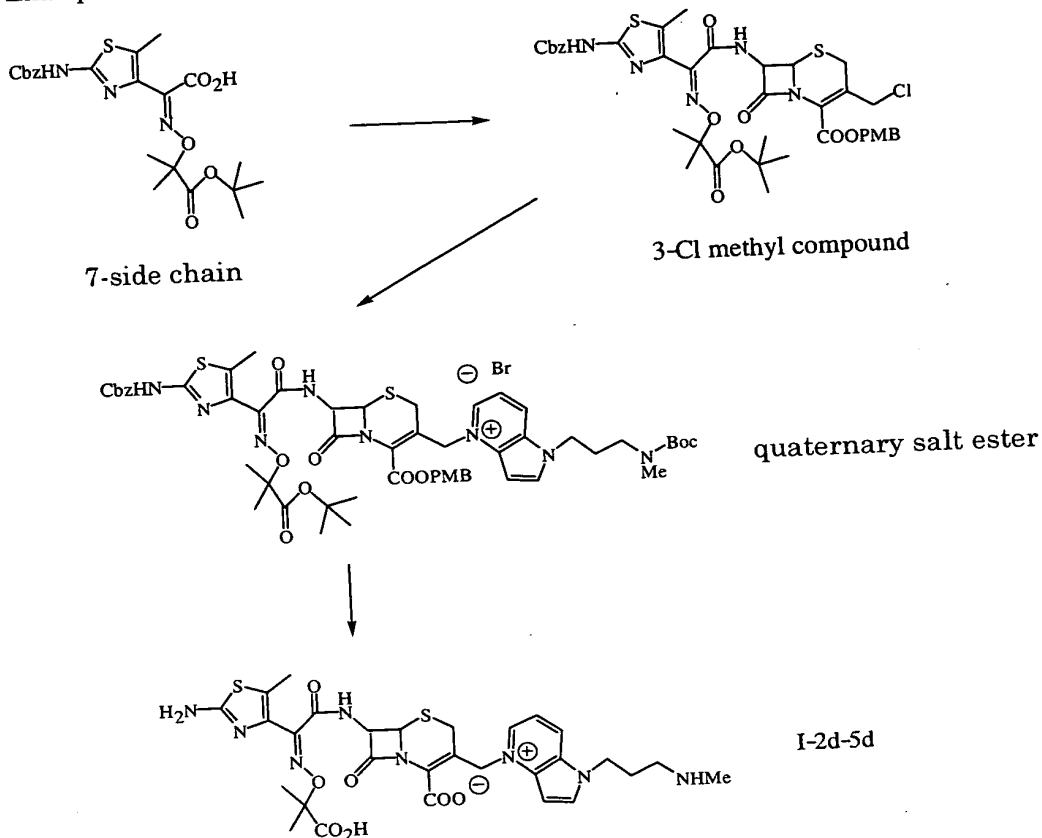
R=
a: H
b: Me
c: (CH₂)₂NHMe
d: (CH₂)₃NHMe

The structure of compound (I) of Examples 1 to 21 are shown below.

|  <p style="text-align: right;">(I)</p> | | | | | |
|---|----------------|----|------------------------------------|--------------------|----|
| Exempl e | Compound No | X | R 1 | R 2 | Z |
| 1 | I-2d-5d | Me | Me | Me | 5d |
| 2 | I-3a-5d | Cl | H | H | 5d |
| 3 | I-3d-1 | Cl | Me | Me | 1 |
| 4 | I-3d-2a | Cl | Me | Me | 2a |
| 5 | I-3d-5d | Cl | Me | Me | 5d |
| 6 | I-3d-6d | Cl | Me | Me | 6d |
| 7 | I-3d-5c | Cl | Me | Me | 5c |
| 8 | I-3e-5d | Cl | Me | H | 5d |
| 9 | I-3f-5d | Cl | H | Me | 5d |
| 10 | I-3g-5d | Cl | Et | H | 5d |
| 11 | I-3h-5d | Cl | H | Et | 5d |
| 12 | I-3i-5d | Cl | iPr | H | 5d |
| 13 | I-3j-5d | Cl | H | iPr | 5d |
| 14 | I-3k-5d | Cl | CH ₂ OH | H | 5d |
| 15 | I-3l-5d | Cl | H | CH ₂ OH | 5d |
| 16 | I-3f-2a | Cl | H | Me | 2a |
| 17 | I-3c-2a | Cl | -(CH ₂) ₃ - | | 2a |
| 18 | I-3c-5d | Cl | -(CH ₂) ₃ - | | 5d |
| 19 | I-3b-5d | Cl | = CH ₂ | | 5d |
| 20 | I-4d-5d | Br | Me | Me | 5d |
| 21 | I-4f-5d | Br | H | Me | 5d |

5 The synthesis method and physical data are shown below. The synthesis was conducted according to the method of Example 2, 5 etc.

Example 1



I-2d-5d :

¹H-NMR (D₂O) δ : 1.46(6H, s), 2.27(3H, s), 2.31(2H, m), 2.69(3H, s), 3.06(2H, m), 3.18

5 and 3.39(2H, ABq, J = 17.7 Hz), 4.52(2H, t, J = 7.2 Hz), 5.18(1H, d, J = 4.8 Hz), 5.55
and 5.69(2H, ABq, J = 15.0 Hz), 5.82(1H, d, J = 4.8 Hz), 7.04(1H, d, J = 3.6 Hz), 7.69(1H,
dd, J = 6.0 and 8.4 Hz), 8.12(1H, d, J = 3.6 Hz), 8.59(1H, d, J = 8.4 Hz), 8.65(1H, d, J =
6.0 Hz).

IR (KBr) cm⁻¹: 3413, 2983, 2458, 1774, 1610, 1498, 1467, 1392, 1359, 1288, 1195, 1162,

10 1122.

MS(ESI): 671⁺(M+H⁺).

Elemental analysis C₂₉H₃₄N₈O₇S₂ · 5.6 H₂O.

Calc. : C, 45.14 ; H, 5.90 ; N, 14.52 ; S, 8.31 (%).

Found : C, 45.15 ; H, 5.32 ; N, 14.36 ; S, 8.49 (%).

15 quaternary salt ester :

¹H-NMR (d₆-DMSO) δ : 1.37(9H, s), 1.38(6H, s), 1.42(9H, s), 2.03(2H, m),

2.41(3H, s), 2.78(3H, brs), 3.18(2H, m), 3.36 and 3.56(2H, m), 3.75(3H,

s), 4.43(2H, m), 5.17(1H, d, J = 5.1 Hz), 5.21(2H, s), 5.22 and 5.29(2H, ABq, J = 11.4 Hz),

5.67 and 5.72(2H, ABq, J = 16.2 Hz), 5.96(1H, dd, J = 5.1 and 8.7 Hz), 6.90(2H, d, J = 8.7 Hz), 6.96(1H, d, J = 3.6 Hz), 7.33(2H, d, J = 8.7 Hz), 7.34-7.45(5H, 7.78(5H, m), 7.78(1H, m), 8.43(1H, d, J = 3.3 Hz), 8.62(1H, d, J = 6.0 Hz), 8.88(1H, d, J = 8.4 Hz), 9.49(1H, d, J = 8.7 Hz), 12.1(1H, brs).

5 IR (KBr) cm^{-1} : 3423, 3089, 2973, 2933, 1791, 1724, 1685, 1556, 1515, 1496, 1454, 1390, 1365, 1299, 1247, 1222, 1174, 1145, 1062, 1027.

MS(ESI): 1081⁺(C₅₄H₆₅N₈O₁₂S₂⁺).

3-chloromethyl compound:

¹H-NMR (CDCl₃) δ : 1.42(9H, s), 1.57(3H, s), 1.58(3H, s), 2.48(3H, s), 3.47 and 3.64(2H, ABq, J = 18.3 Hz), 3.81(3H, s), 4.44 and 4.55(2H, ABq, J = 11.7 Hz), 5.04(1H, d, J = 5.1 Hz), 5.20 and 5.26(2H, ABq, J = 12.0 Hz), 5.25(2H, s), 6.04(1H, dd, J = 5.1 and 9.3 Hz), 6.90(2H, d, J = 9.0 Hz), 7.35(2H, d, J = 9.0 Hz), 7.30-7.40(5H, m), 7.90(1H, d, J = 9.3 Hz), 8.38(1H, brs).

15 IR (KBr) cm^{-1} : 3386, 3283, 2979, 2937, 1789, 1726, 1692, 1613, 1557, 1515, 1455, 1383, 1367, 1300, 1247, 1224, 1142, 1094, 1061.

MS(ESI): 828⁺(M+H⁺).

Elemental analysis C₃₈H₄₂ClN₅O₁₀S₂ · 0.05 CHCl₃ · 0.7 H₂O.

Calc. : C, 53.96 ; H, 5.17 ; N, 8.27 ; S, 7.57 ; Cl, 4.81 (%).

Found : C, 54.03 ; H, 5.14 ; N, 8.16 ; S, 7.29 ; Cl, 4.81 (%).

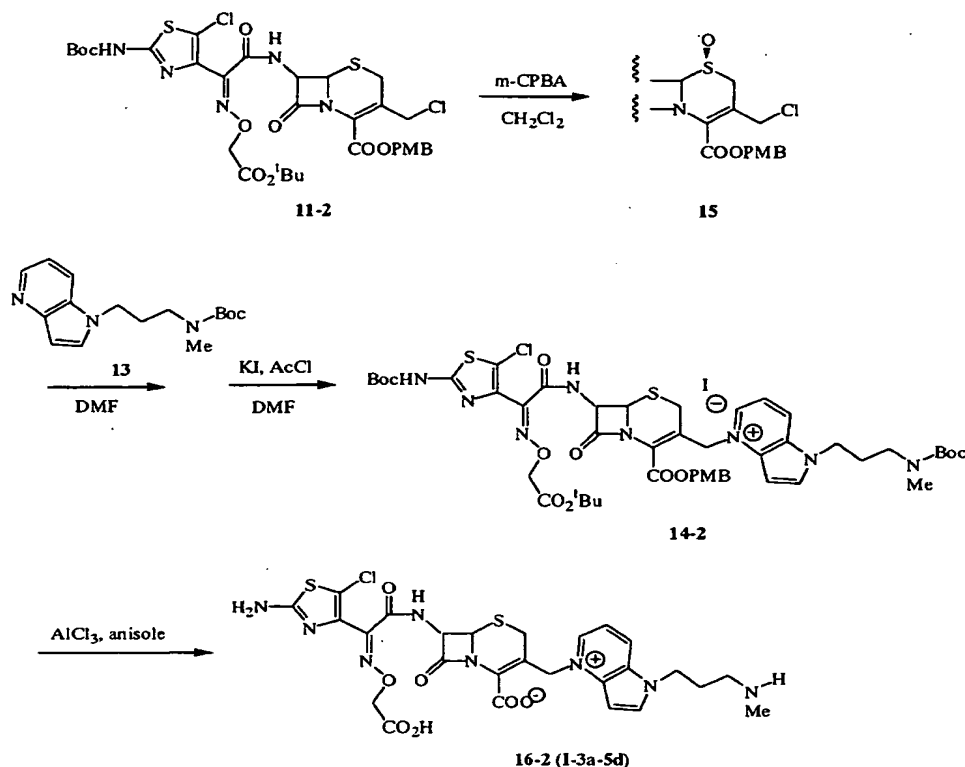
20 7-side chain

¹H-NMR (d₆-DMSO) δ : 1.39(9H, s), 1.41(6H, s), 2.43(3H, s), 5.22(2H, s), 7.30-7.40(5H, m), 12.0(1H, brs).

IR (KBr) cm^{-1} : 3430, 3193, 2981, 2937, 1731, 1614, 1596, 1562, 1455, 1392, 1369, 1299, 1228, 1187, 1141, 1062.

25 MS(ESI): 478⁺(M+H⁺).

Example 2



- (1) A solution of compound 11-2 (1.20g 1.53mmol) in CH_2Cl_2 12ml was cooled to -50°C in nitrogen atmosphere, to which was added 2ml solution of 65% m-CPBA (366mg 0.9eq) and the mixture was stirred at -50°C to -40°C for 15 min. The reaction mixture was poured to a saturated $\text{Na}_2\text{S}_2\text{O}_3$ solution and extracted with CHCl_3 . The obtained organic layer was washed with a saturated NaHCO_3 aq. solution and brine, dried over anhydrous MgSO_4 , and concentrated under reduced pressure. The obtained compound 15 (1.18g 1.47mmol) was dissolved to DMF 2ml under nitrogen atmosphere, to which were added a solution of NaBr (303mg 2eq) and compound 13 (627mg 1.55eq) in DMF 2ml. The mixture was stirred at room temperature for 5 hr and allowed to stand overnight at 4°C . DMF 20ml and KI 1.7g were added thereto under nitrogen atmosphere and the mixture was cooled to -50°C . AcCl 0.523ml was added dropwise and the mixture was stirred at -50°C for 1hr and at -50°C to -10°C for 1.5 hr. The reaction solution was added dropwise to a 5% NaCl solution containing $\text{Na}_2\text{S}_2\text{O}_3$ 1g under ice-cooling to give precipitates. The precipitates were collected by filtration and dried using P_2O_5 under reduced pressure to give compound 14-2 (1.59g) as powder.
- compound 14-2

¹H-NMR (d₆-DMSO) δ : 1.40(9H, s), 1.46(18H, s), 2.03(2H, m), 2.78(3H, brs), 3.18(2H, t, J = 7.2 Hz), 3.27 and 3.43(2H, ABq, J = 18.3 Hz), 3.75(3H, s), 4.43(2H, t, J = 6.6 Hz), 4.55(2H, s), 5.18(1H, d, J = 4.8 Hz), 5.21 and 5.28(2H, ABq, J = 12.0 Hz), 5.65 and 5.73(2H, ABq, J = 15.3 Hz), 5.95(1H, dd, J = 4.8 and 8.7 Hz), 6.89(2H, d, J = 8.7 Hz),
5 7.00(1H, d, J = 3.3 Hz), 7.35(2H, d, J = 8.7 Hz), 7.78(1H, dd, J = 6.3 and 8.1 Hz), 8.43(1H, d, J = 3.3 Hz), 8.60(1H, d, J = 6.3 Hz), 8.88(1H, d, J = 8.1 Hz), 9.65(1H, d, J = 8.7 Hz), 12.1(1H, brs).

IR (KBr) cm⁻¹: 3427, 3058, 2976, 2933, 1791, 1718, 1686, 1630, 1613, 1584, 1550, 1515, 1496, 1455, 1393, 1368, 1300, 1247, 1156, 1080, 1063, 1022.

10 MS(ESI): 1039⁺(C₄₈H₆₀ClN₈O₁₂S₂⁺).

compound 11-2

¹H-NMR (CDCl₃) δ : 1.44(9H, s), 1.53(9H, s), 3.47 and 3.63(2H, ABq, J = 18.0 Hz), 3.82(3H, s), 4.45(2H, s), 4.68 and 4.75(2H, ABq, J = 16.8 Hz), 5.05(1H, d, J = 4.8 Hz), 5.20 and 5.27(2H, ABq, J = 12.0 Hz), 5.98(1H, dd, J = 4.8 and 9.3 Hz), 6.91(2H, d, J =
15 8.7 Hz), 7.35(2H, d, J = 8.7 Hz), 8.11(1H, brs), 8.49(1H, d, J = 9.3 Hz).

IR (KBr) cm⁻¹: 3382, 3277, 2979, 2935, 2837, 1791, 1722, 1613, 1551, 1515, 1455, 1369, 1302, 1246, 1157, 1085, 1062, 1036, 1021.

MS(FAB): 786⁺(M+H⁺).

HR-MS(FAB): calcd for C₃₂H₃₈Cl₂N₅O₁₀S₂ 786.1437 found 786.1434 .

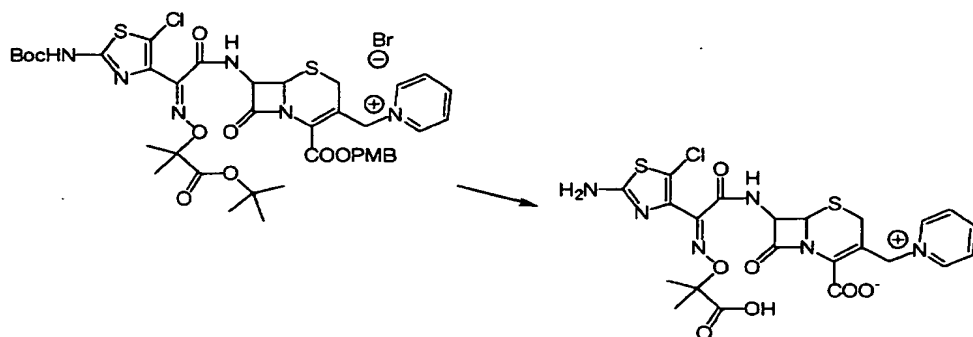
20 (2) Compound 14-2 (1.59g, about 1.47mmol) was deprotected according to Example 5(3) to give compound 16-2 (I-3a-5d, 270mg).

¹H-NMR (d₆-DMSO) δ : 1.40(9H, s), 1.46(18H, s), 2.03(2H, m), 2.78(3H, brs), 3.18(2H, t, J = 7.2 Hz), 3.27 and 3.43(2H, ABq, J = 18.3 Hz), 3.75(3H, s), 4.43(2H, t, J = 6.6 Hz), 4.55(2H, s), 5.18(1H, d, J = 4.8 Hz), 5.21 and 5.28(2H, ABq, J = 12.0 Hz), 5.65 and
25 5.73(2H, ABq, J = 15.3 Hz), 5.95(1H, dd, J = 4.8 and 8.7 Hz), 6.89(2H, d, J = 8.7 Hz), 7.00(1H, d, J = 3.3 Hz), 7.35(2H, d, J = 8.7 Hz), 7.78(1H, dd, J = 6.3 and 8.1 Hz), 8.43(1H, d, J = 3.3 Hz), 8.60(1H, d, J = 6.3 Hz), 8.88(1H, d, J = 8.1 Hz), 9.65(1H, d, J = 8.7 Hz), 12.1(1H, brs).

IR (KBr) cm⁻¹: 3427, 3058, 2976, 2933, 1791, 1718, 1686, 1630, 1613, 1584, 1550, 1515,
30 1496, 1455, 1393, 1368, 1300, 1247, 1156, 1080, 1063, 1022.

MS(ESI): 1039⁺(C₄₈H₆₀ClN₈O₁₂S₂⁺).

Example 3



I-3d-1 :

$^1\text{H-NMR}$ (D_2O) δ : 1.54(6H, s), 3.22 and 3.64(2H, ABq, $J = 17.7$ Hz), 5.28(1H, d, $J = 4.8$ Hz), 5.34 and 5.58(2H, ABq, $J = 14.4$ Hz), 5.88(1H, d, $J =$
 4.8 Hz), 8.09(2H, t like), 8.58(1H, t like), 8.96(2H, d, $J = 6.0$ Hz).

IR (KBr) cm^{-1} : 3417, 3058, 2989, 2938, 2524, 1778, 1673, 1625, 1536, 1486, 1386, 1340, 1157.

MS(ESI): 581 $^+$ ($\text{M}+\text{H}^+$).

Elemental analysis $\text{C}_{22}\text{H}_{21}\text{ClN}_6\text{O}_7\text{S}_2 \cdot 2.9 \text{H}_2\text{O}$.

Calc. : C, 41.73 ; H, 4.27 ; N, 13.27 ; Cl, 5.60 ; S, 10.13 (%).

Found : C, 41.74 ; H, 3.99 ; N, 13.16 ; Cl, 5.53 ; S, 10.20 (%).

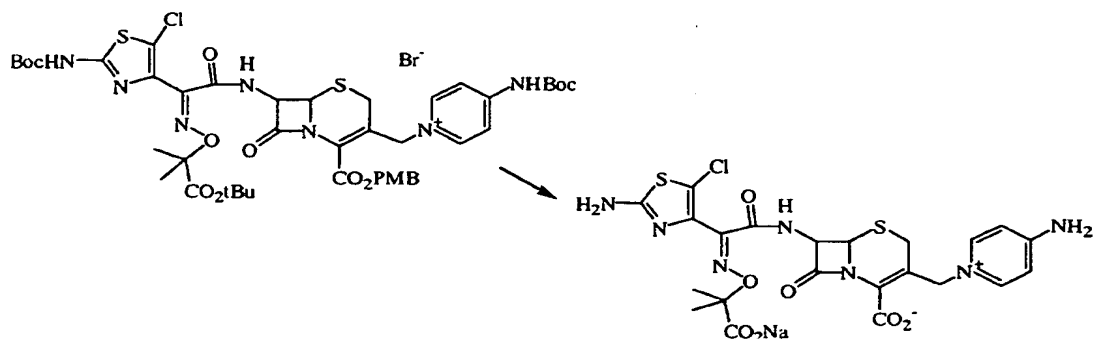
quaternary salt ester :

$^1\text{H-NMR}$ ($\text{d}_6\text{-DMSO}$) δ : 1.37(9H, s), 1.42(3H, s), 1.44(3H, s), 1.46(9H, s),
 3.51(2H, brs), 3.77(3H, s), 5.20 and 5.26(2H, ABq, $J = 12.0$ Hz), 5.22(1H, d, $J = 5.1$ Hz),
 5.58(2H, brs), 5.98(1H, dd, $J = 5.1$ and 9.0 Hz), 6.93(2H, d, $J = 8.4$ Hz), 7.35(2H, d, $J =$
 8.4 Hz), 8.20(2H, t like), 8.66(1H, t like), 8.99(2H, d, $J = 5.7$ Hz), 9.57(1H, d, $J = 9.0$ Hz),
 12.1(1H, brs).

IR (KBr) cm^{-1} : 3428, 3054, 2979, 2935, 1791, 1718, 1629, 1614, 1548, 1515, 1481, 1455, 1392, 1369, 1299, 1247, 1153, 1064, 1029.

MS(ESI): 857 $^+$ ($\text{C}_{39}\text{H}_{46}\text{ClN}_6\text{O}_{10}\text{S}_2^+$).

Example 4



I-3d-2a :

$^1\text{H-NMR}$ (D_2O) δ : 1.40(6H, s), 3.18 and 3.55(2H, ABq, $J = 17.7$ Hz), 4.88 and 5.02(2H, ABq, $J = 14.7$ Hz), 5.23(1H, d, $J = 4.8$ Hz), 5.84(1H, d, $J = 4.8$ Hz), 6.83 and 8.05(4H, A2B2q, $J = 7.5$).

IR (KBr) cm^{-1} : 3400, 3189, 2993, 1770, 1654, 1604, 1537, 1398, 1361, 1165 .

Elemental analysis $\text{C}_{27}\text{H}_{21.2}\text{N}_7\text{O}_7\text{S}_2\text{ClNa}_{0.8} \cdot 5\text{H}_2\text{O}$ として.

Calc. : C,37.55; H,4.47; N,13.93; S,9.11; Cl,5.04; Na,2.61 (%).

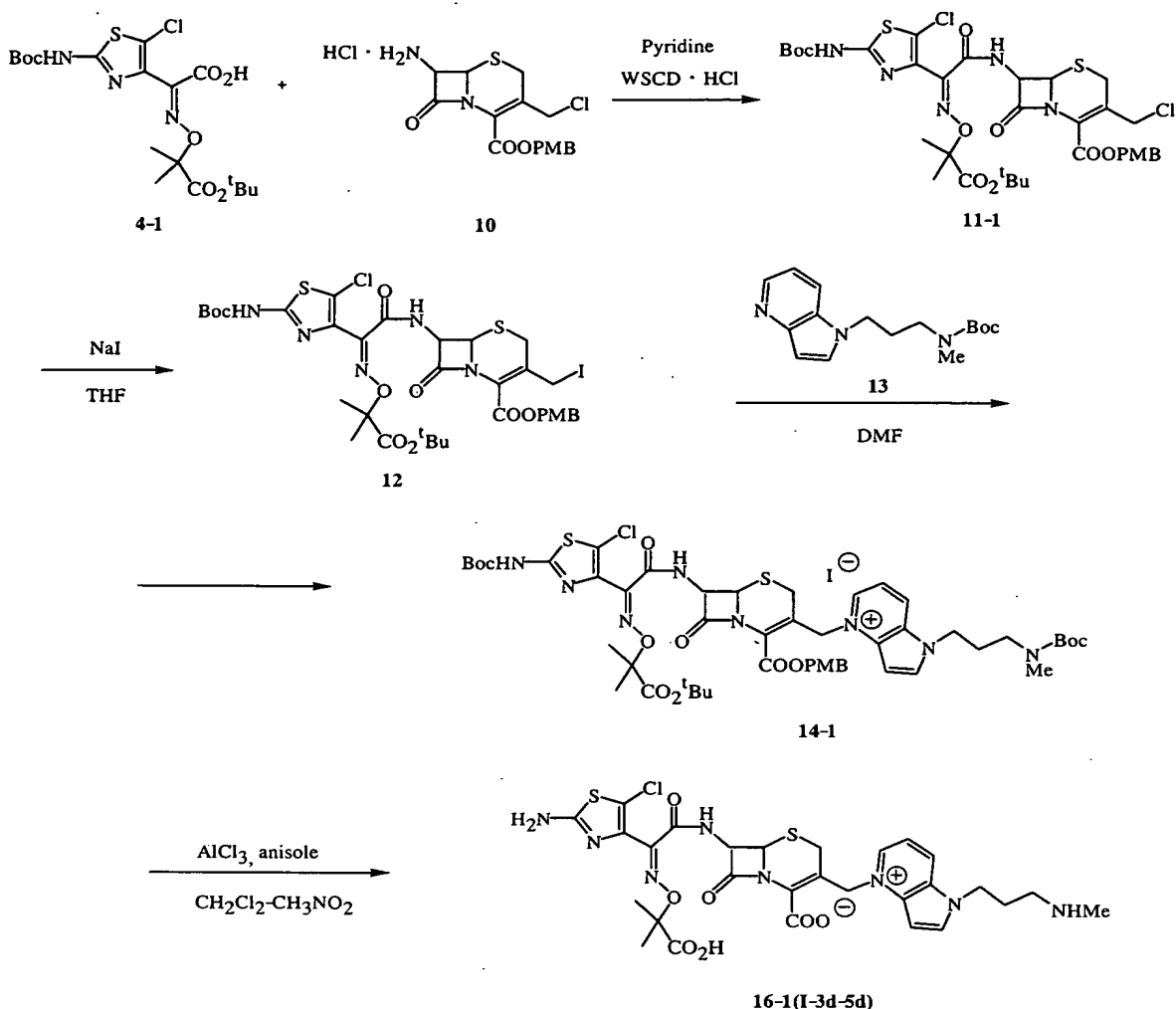
Found : C,37.34; H,4.28; N,13.73; S,9.07; Cl,4.97; Na,2.70 (%).

10 quaternary salt ester :

$^1\text{H-NMR}$ (CDCl_3) δ : 1.43(9H, s), 1.51(9H, s), 1.55(9H, s), 1.58(3H, s), 1.59(3H, s), 3.35 and 3.92(2H, ABq, $J = 19.2$ Hz), 3.82(3H, s), 5.24 ~ 5.30(3H, m), 5.31 and 5.57(2H, Abq, $J = 14.4$ Hz), 6.01(1H, dd, $J = 4.8, 8.7$ Hz), 6.90 and 7.36(4H, A2B2q, $J = 9$ Hz), 8.04~8.12(3H, m), 8.35(1H, br s) , 8.63(2H, $J = 7.5$ Hz), 8.98(1H, s) .

15 IR (KBr) cm^{-1} : 3422, 3274, 2979, 2934, 1794, 1719, 1641, 1530, 1457, 1369, 1299, 1246, 1146, 842 .

Example 5



(1) To a solution of compound 4-1 (10.3, 22.2mmol) obtained in Reference Example 1 and compound 10 (9.90g 24.4mmol) in dry DMA 100ml, were added WSCD · HCl (5.11g 1.2eq) and pyridine (1.80ml, 1.0eq) under ice-cooling and the mixture was stirred at room temperature for 1 hr. The reaction mixture was poured to ice water 300ml and extracted with AcOE (200ml×2). The obtained organic layer washed with brine, dried over anhydrous MgSO₄, and concentrated in vacuum. Purification with silica gel column chromatography, followed by concentration in vacuum, gave compound 11-1 (13.7g) as foam.

¹H-NMR (CDCl₃) δ : 1.42(9H, s), 1.52(9H, s), 1.60(6H, s), 3.48 and 3.65(2H, ABq, J = 18.0 Hz), 3.82(3H, s), 4.45 and 4.55(2H, ABq, J = 11.7 Hz), 5.04(1H, d, J = 5.1 Hz), 5.20 and 5.27(2H, ABq, J = 12.0 Hz), 6.03(1H, dd, J = 5.1 and 9.3 Hz), 6.91(2H, d, J = 8.7 Hz), 7.35(2H, d, J = 8.7 Hz), 8.03(1H, d, J = 9.3 Hz), 8.13(1H, brs).

IR (KBr) cm⁻¹: 3396, 3284, 2979, 2937, 2836, 1791, 1722, 1614, 1550, 1515, 1455, 1384,

1369, 1301, 1247, 1155, 1035.

MS(ESI): 814⁺(M+H⁺).

Elemental analysis $C_{34}H_{41}Cl_2N_5O_{10}S_2 \cdot 0.2 CHCl_3 \cdot 0.4 H_2O$.

Calc. : C, 48.56 ; H, 5.00 ; N, 8.28 ; S, 7.58 ; Cl, 10.90 (%).

5 Found : C, 48.51 ; H, 4.85 ; N, 8.11 ; S, 7.56 ; Cl, 11.00 (%).

(2) To a solution of compound 11-1 (5.0g 6.14mmol) in THF 50ml which was cooled to 15°C under nitrogen atmosphere, was added NaI 2.76g (3eq) and the mixture was stirred at 15°C for 30 min. The reaction solution was poured to ice water 150ml and extracted with AcOE. The obtained organic layer was washed with a saturated

10 $Na_2S_2O_3$ aq. solution and brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure to give compound 12 (5.51g) as a form. To a solution of compound 12 (2.72g 3.0mmol) in DMF 12ml, was added a solution of compound 13 (868mg 1eq) in DMF 3ml under nitrogen atmosphere. After stirring at room temperature for 1hr, the reaction mixture was added dropwise to a 5% NaCl solution under ice-cooling to
15 give pale yellow precipitates, which was collected by filtration. Drying with P_2O_5 under reduced pressure gave compound 14-1 (3.26g) as powder.

¹H-NMR (d_6 -DMSO) δ : 1.37(9H, s), 1.43(6H, s), 1.46(18H, s), 2.03(2H, m), 2.78(3H, brs), 3.17(2H, m), 3.28 and 3.39(2H, ABq, J = 16.2 Hz), 3.76(3H, s), 4.43(2H, m),
20 5.18(1H, d, J = 5.1 Hz), 5.22 and 5.30(2H, ABq, J = 11.7 Hz), 5.70(2H, brs), 5.95(1H, dd, J = 5.1 and 8.7 Hz), 6.90(2H, d, J = 8.7 Hz), 6.95(1H, d, J = 3.3 Hz), 7.33(2H, d, J = 8.7 Hz), 7.78(1H, dd, J = 5.7 and 8.4 Hz), 8.43(1H, d, J = 3.3 Hz), 8.63(1H, d, J = 5.7 Hz), 8.88(1H, d, J = 8.4 Hz), 9.58(1H, d, J = 8.7 Hz), 12.1(1H, brs).

IR (KBr) cm^{-1} : 3423, 2977, 2935, 1789, 1718, 1685, 1629, 1612, 1550, 1515, 1496, 1455, 1392, 1367, 1299, 1249, 1153.

25 MS(ESI): 1067⁺($C_{50}H_{64}ClN_8O_{12}S_2^+$).

(3) To a solution of compound 14-1 (3.20g) in $MeNO_2$ 30 ml and anisole 30 ml, was added a $AlCl_3$ - $MeNO_2$ solution (1.5M, 21 ml) in nitrogen atmosphere under ice-cooling and the mixture was stirred for 1 hr. Ice, 1N HCl, CH_3CN and Et_2O were added thereto, and the water layer was separated and concentrated in vacuum. Purification
30 with HP-20 chromato, followed by lyophilization, gave compound 16-1 (I-3d-5d, colorless powder, 900 mg).

¹H-NMR (D_2O) δ : 2.30(2H, m), 2.68(3H, s), 3.05(2H, m), 3.15 and 3.38 (2H, ABq, J = 17.7 Hz), 4.52(2H, t, J = 6.9 Hz), 4.54(2H, s), 5.16(1H, d, J = 4.8 Hz), 5.56 and 5.67(2H, ABq, J = 15.0 Hz), 5.83(1H, d, J = 4.8 Hz), 7.04(1H, d, J = 3.6 Hz), 7.68(1H, dd, J = 6.0
35 and 8.1 Hz), 8.12(1H, d, J = 3.6 Hz), 8.59(1H, d, J = 8.1 Hz), 8.65(1H, d, J = 6.0 Hz).

IR (KBr) cm^{-1} : 3394, 2817, 1773, 1604, 1539, 1498, 1466, 1391, 1361, 1317, 1163, 1121., 1055, 1033.

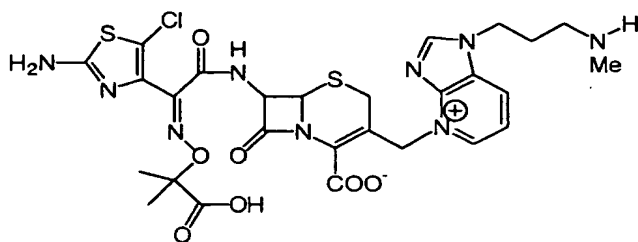
MS(ESI):663⁺(M+H⁺).

Elemental analysis $\text{C}_{26}\text{H}_{27}\text{ClN}_8\text{O}_7\text{S}_2 \cdot 3.7 \text{ H}_2\text{O}$.

5 Calc. : C,42.79 ; H,4.75 ; N,15.35 ; Cl,4.86; S,8.79 (%).

Found : C,42.78 ; H,4.66 ; N,15.42 ; Cl,4.81; S,9.02 (%).

Example 6



10 I-3d-6d :

¹H-NMR(D₆-DMSO-D₂O) δ : 1.38(6H, brs), 2.23(2H, brs), 2.48(3H, s), 2.92(2H, brs), 3.13 and 3.52 (2H, ABq, J = 17.4 Hz), 4.55(2H, brs), 5.06(1H, d, J = 4.8 Hz), 5.59 and 5.70(2H, ABq, J = 12.9 Hz), 5.79(1H, d, J = 4.8 Hz), 7.71(1H, t like), 8.82(1H, d, J = 7.8), 9.04(1H, s), 9.19(1H, d, J = 5.1 Hz).

15 IR(KBr) cm^{-1} :3421, 2460, 1772, 1610, 1538, 1488, 1465, 1394, 1359, 1315, 1234, 1159.

MS(ESI):692⁺(M+H⁺).

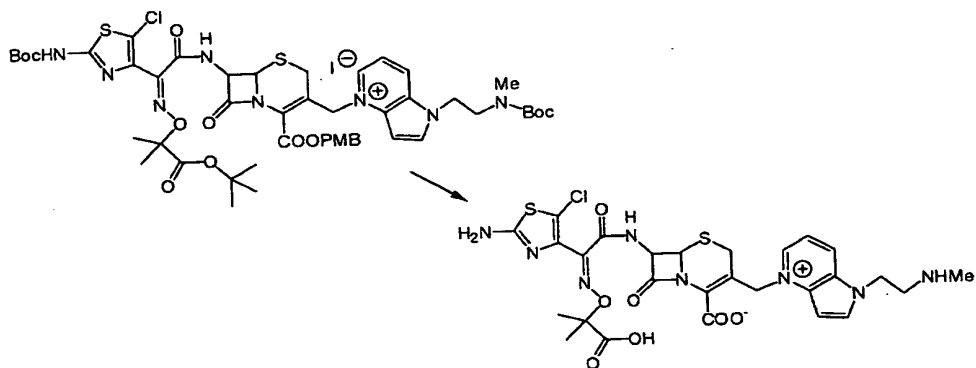
Elemental analysis $\text{C}_{27}\text{H}_{30}\text{ClN}_9\text{O}_7\text{S}_2 \cdot 5.3(\text{H}_2\text{O})$.

Calc. : C,40.98 ; H,5.18 ; N,15.93 ; Cl,4.93 ; S,8.10 (%).

Found : C,40.70 ; H,4.88 ; N,15.74 ; Cl,4.94 ; S,7.97 (%).

20

Example 7



I-3d-5c :

$^1\text{H-NMR}$ (D_2O) δ : 1.48(6H, s), 2.73(3H, s), 3.17 and 3.40(2H, ABq, $J = 17.7$ Hz), 3.61(2H, t, $J = 6.0$ Hz), 4.79(2H, t, $J = 6.0$ Hz), 5.17(1H, d, $J = 5.1$ Hz), 5.57 and 5.69(2H, ABq, $J = 15.0$ Hz), 5.81(1H, d, $J = 5.1$ Hz), 7.10(1H, d, $J = 3.3$ Hz), 7.70(1H, dd, $J = 6.3$ and 8.1 Hz), 8.14(1H, d, $J = 3.3$ Hz), 8.61(1H, d, $J = 8.1$ Hz), 8.69(1H, d, $J = 6.3$ Hz).
 IR (KBr) cm^{-1} : 3401, 2987, 2451, 1772, 1606, 1538, 1500, 1467, 1396, 1361, 1288, 1159, 1120.

MS(ESI): 677 $^+$ ($\text{M}+\text{H}^+$).

Elemental analysis $\text{C}_{27}\text{H}_{29}\text{ClN}_8\text{O}_7\text{S}_2 \cdot 6.5 \text{H}_2\text{O}$.

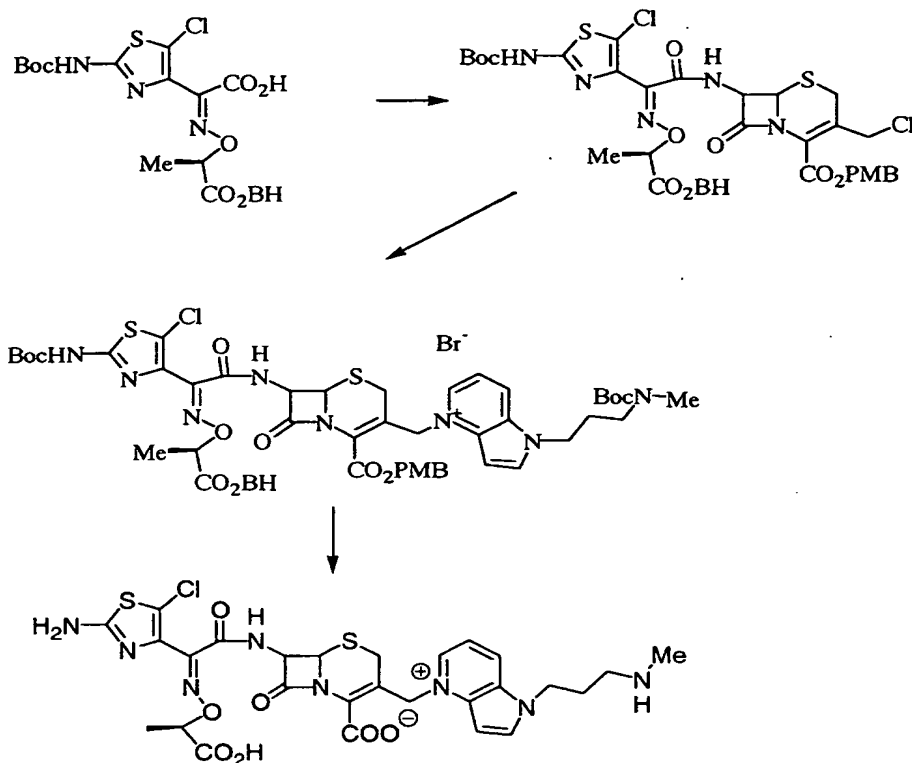
Calc. : C, 40.83 ; H, 5.33 ; N, 14.11 ; Cl, 4.46 ; S, 8.07 (%).

Found : C, 40.82 ; H, 5.14 ; N, 14.12 ; Cl, 4.57 ; S, 8.03 (%).

quaternary salt ester:

$^1\text{H-NMR}$ (d_6 -DMSO) δ : 1.37(9H, s), 1.39(3H, s), 1.43(3H, s), 1.46(18H, s), 2.80(3H, brs), 3.27 and 3.39(2H, m), 3.59(2H, m), 3.76(3H, s), 4.60(2H, brs), 5.17(1H, d, $J = 5.1$ Hz), 5.23 and 5.31(2H, ABq, $J = 12.0$ Hz), 5.72(2H, brs), 5.96(1H, dd, $J = 5.1$ and 8.7 Hz), 6.92(2H, d, $J = 8.4$ Hz), 7.02(1H, d, $J = 3.6$ Hz), 7.36(2H, d, $J = 8.4$ Hz), 7.82(1H, m), 8.31(1H, d, $J = 3.6$ Hz), 8.67(1H, m), 8.85(1H, m), 9.58(1H, d, $J = 8.7$ Hz), 12.1(1H, brs).

Example 8



I-3e-5d :

¹H-NMR (D₂O) δ : 1.40(3H, d, J = 6.9 Hz), 2.31(2H, q like), 2.68(3H, s), 3.05(2H, t like),
 3.14 and 3.39(2H, ABq, J = 17.7 Hz), 4.52(2H, t like), 4.61(1H, q, J = 6.9 Hz), 5.19(1H,
 5 d, J = 4.8 Hz), 5.57 and 5.67(2H, ABq, J = 15 Hz), 5.80(1H, d, J = 4.5 Hz), 7.06(1H, d, J =
 3.6), 7.69(1H, dd, J = 6.0, 8.1 Hz), 8.12(1H, d, J = 3.6 Hz), 8.59(1H, d, J = 8.1 Hz),
 8.64(1H, d, J = 6.0 Hz).

IR (KBr) cm⁻¹: 3411, 1774, 1606, 1539, 1498, 1392, 1363, 1034, 759 .

Positive ESIMS: m/z 677 [M+H]⁺ . Negative ESIMS: m/z 675 [M-H]⁻ .

10 Elemental analysis as C₂₇H₂₉N₈O₇S₂Cl · 6.2H₂O

Calc. : C,41.11; H,5.29; N,14.20; S,8.13; Cl,4.49 (%).

Found : C,40.99; H,5.07; N,14.15; S,8.21; Cl,4.76 (%).

quaternary salt ester :

¹H-NMR (CDCl₃) δ : 1.48(9H, s), 1.51(9H, s), 1.60(3H, d, J = 7.2 Hz), 2.22(2H, t like),
 15 2.91(3H, s), 3.17 and 3.73(2H, ABq, J = 18.6 Hz), 3.37(2H, t like), 3.81(3H, s), 4.44(2H, t
 like), 5.03(1H, q, J = 7.2 Hz), 5.17(1H, d, J = 5.1 Hz), 5.24 and 5.30(2H, ABq, J = 11.7
 Hz), 5.63 and 5.75(2H, ABq, J = 15 Hz), 6.01(1H, dd, J = 5.1, 9 Hz), 6.87 (2H, d, J = 8.7
 Hz), 6.88(1H, s), 7.24~ 7.35 (12H, m), 7.59(1H, dd, J = 6, 8.1 Hz), 7.78(1H, d, J = 9 HZ),

8.24(1H, m), 8.34(1H, br s), 8.48(1H, d, J = 8.1 Hz), 8.53(1H, d, J = 6.0 Hz) .

IR (KBr) cm^{-1} : 3430, 3091, 3060, 1793, 1718, 1684, 1630, 1549, 1516, 1367, 1247, 1153, 1034, 754, 702 .

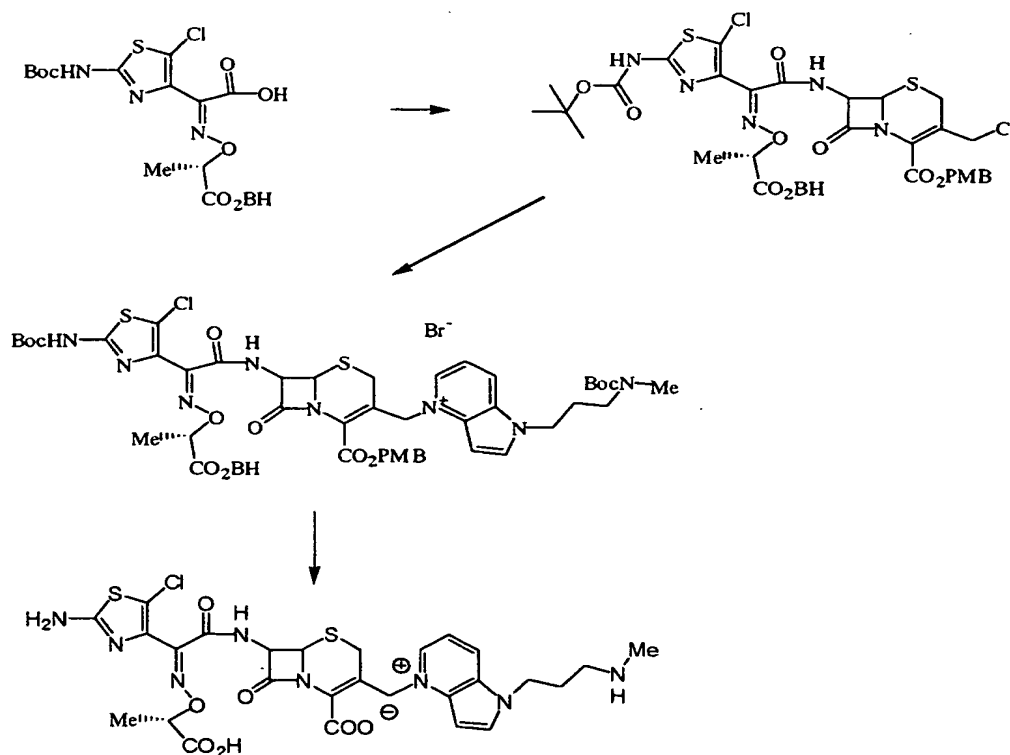
3-chloromethyl compound:

- 5 $^1\text{H-NMR}$ (CDCl_3) δ : 1.53(9H, s), 1.65(3H, d, J = 7.2 Hz), 3.23 and 3.47(2H, ABq, J = 18.3 Hz), 3.82(3H, s), 4.39 and 4.55(2H, ABq, J = 12 Hz), 4.99(1H, d, J = 5.1 Hz), 5.10(1H, q, J = 7.2 Hz), 5.21 and 5.27(2H, ABq, J = 12 Hz), 5.99(1H, dd, J = 5.1, 9.9 Hz), 6.91(3H, m), 7.16~ 7.37 (12H, m), 7.76 (1H, d, J = 9.9 Hz), 8.20(1H, br s).
10 IR (KBr) cm^{-1} : 3373, 3286, 2979, 2937, 1791, 1720, 1612, 1550, 1515, 1248, 1155, 1035, 700 .

7-side chain (NEt_3 salt) :

- $^1\text{H-NMR}$ (CDCl_3) δ : 1.50(9H, s), 1.51(3H, d, J = 7.2 Hz), 4.94(1H, q, J = 7.2), 6.89(1H, s), 7.23 ~ 7.35(10H, m).
IR (KBr) cm^{-1} : 3429, 2981, 2937, 1739, 1714, 1612, 1556, 1250, 1157, 1036, 964, 700 ,
15 Positive ESIMS: m/z 560 $[\text{M}+\text{H}]^+$, m/z 582 $[\text{M}+\text{Na}]^+$.
Negative ESIMS: m/z 558 $[\text{M}-\text{H}]^-$, m/z 580 $[\text{M}+\text{Na}-2\text{H}]^-$.

Example 9



I-3f-5d :

¹H-NMR (D₂O) δ : 1.43 (3H, d, J = 7.2 Hz), 2.31(2H, q like), 2.68(3H, s), 3.05(2H, t, J = 8 Hz), 3.18 and 3.37(2H, ABq, J = 18 Hz), 4.53(2H, t like), 4.65 (1H, q, J = 7.2 Hz), 5.17(1H, d, J = 4.8 Hz), 5.54 and 5.70(2H, ABq, J = 15 Hz), 5.86(1H, d, J = 4.5 Hz),
5 7.03(1H, d, J = 3.6 Hz), 7.69(1H, dd, J = 6, 8.4 Hz), 8.13(1H, d, J = 3.6 Hz), 8.60(1H, d, J = 8.4 Hz), 8.64(1H, d, J = 6 Hz).

IR (KBr) cm⁻¹: 3398, 1775, 1603, 1541, 1392, 1363, 1320, 1286, 1033, 762.

Positive ESIMS: m/z 677 [M+H]⁺ . Negative ESIMS: m/z 675 [M-H]⁻ .

Elemental analysis as C₂₇H₂₉N₈O₇S₂Cl · 6.2H₂O.

10 Calc. : C, 41.11; H, 5.29; N, 14.20; S, 8.13; Cl, 4.49 (%).

Found : C, 40.88; H, 4.88; N, 14.23; S, 8.05; Cl, 4.57 (%).

quaternary salt ester :

¹H-NMR (CDCl₃) δ : 1.48(9H, s), 1.51(9H, s), 1.62(3H, d, J = 7.2 Hz), 2.21(2H, m), 2.91(3H, s), 3.24 and 3.82(2H, ABq, J = 18.9 Hz), 3.36(2H, m), 3.81(3H, s), 4.43(2H, t
15 like), 5.09(1H, q, J = 7.2 Hz), 5.16(1H, d, J = 5.1 Hz), 5.24 and 5.31(2H, ABq, J = 11.7 Hz), 5.58 and 5.75(2H, ABq, J = 14.7 Hz), 5.99(1H, dd, J = 5.1, 8.7 Hz), 6.86(1H, s), 6.87(2H, d, J = 8.7 Hz), 7.00(1H, br s), 7.24 - 7.38(12H, m), 7.55(1H, t like), 7.78(H, d, J = 8.7 Hz), 8.25(1H, br s), 8.47(1H, d, J = 10.2 Hz), 8.50(1H, d, J = 6 Hz).

3-chloromethyl compound:

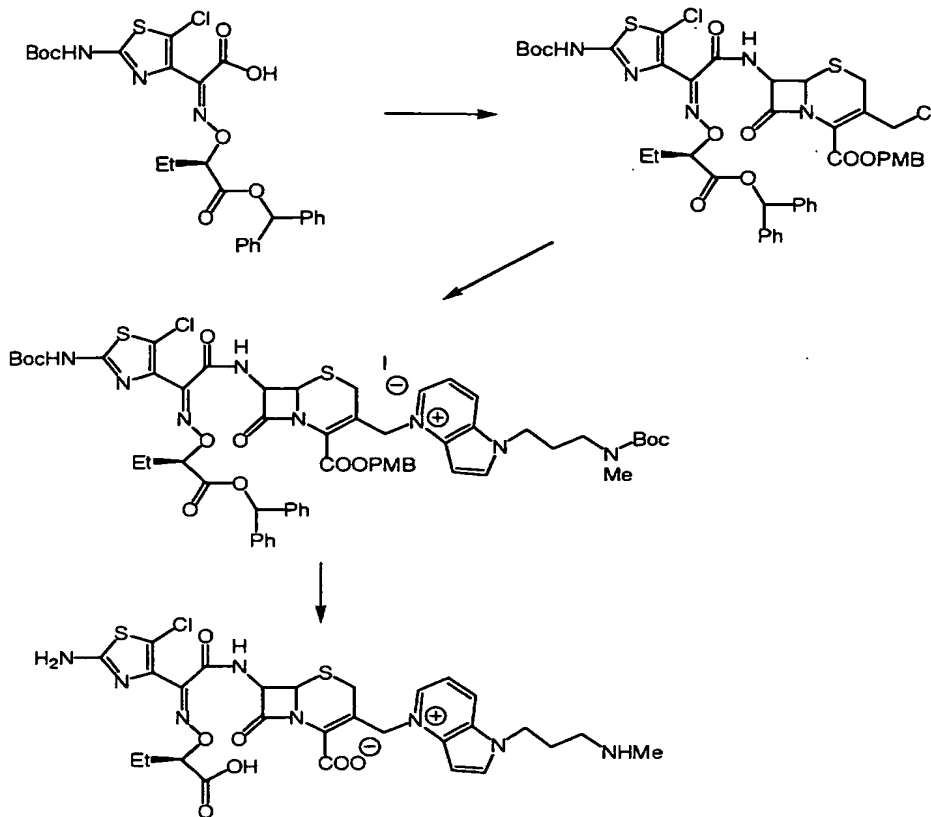
20 ¹H-NMR (CDCl₃) δ : 1.53(9H, s), 1.64(6H, d, J = 7.2 Hz), 3.39 and 3.58(2H, ABq, J = 18.3 Hz), 3.81(3H, s), 4.42 and 4.59(2H, ABq, J = 12 Hz), 4.97(1H, d, J = 5.1 Hz), 5.08(1H, q, J = 7.2 Hz), 5.20 and 5.27(2H, ABq, J = 11.7 Hz), 6.01(1H, dd, J = 5.1, 9.3 Hz), 6.88- 6.91(3H, m), 7.06-7.35(12H, m), 7.85(1H, d, J = 9.3 Hz), 8.15(1H, br s).

IR (KBr) cm⁻¹: 3281, 2980, 2935, 2836, 1790, 1719, 1612, 1552, 1515,
25 1454, 1369, 1247, 1155, 1035, 700 .

7-side chain :

¹H-NMR (CDCl₃) δ : 1.47(9H, s), 1.49(3H, J = 7.2 Hz), 4.99(1H, q, J = 7.2 Hz) .

Example 10



I-3g-5d :

$^1\text{H-NMR}$ (D_2O) δ : 0.90(3H, t, J = 7.5 Hz), 1.79(2H, quintet-like), 2.31(2H, quintet-like), 2.69(3H, s), 3.05(2H, t, J = 8.1 Hz), 3.12 and 3.39 (2H, ABq, J = 18.0 Hz), 4.45(1H, t, J = 6.6 Hz), 4.52(2H, t, J = 7.2 Hz), 5.19(1H, d, J = 4.8 Hz), 5.58 and 5.66(2H, ABq, J = 14.7 Hz), 5.78(1H, d, J = 4.8 Hz), 7.06(1H, d, J = 3.3 Hz), 7.69(1H, dd, J = 6.0 and 8.1 Hz), 8.12(1H, d, J = 3.3 Hz), 8.59(1H, d, J = 8.1 Hz), 8.65(1H, d, J = 6.0 Hz).

IR (KBr) cm^{-1} : 3397, 2967, 1774, 1604, 1537, 1497, 1459, 1390, 1361, 1315, 1159, 1120, 1051, 1031.

MS(ESI): 691 $^+$ ($\text{M}+\text{H}^+$).

Elemental analysis as $\text{C}_{28}\text{H}_{31}\text{ClN}_8\text{O}_7\text{S}_2 \cdot 4.9 \text{ H}_2\text{O}$.

Calc. : C, 43.15 ; H, 5.28 ; N, 14.38 ; Cl, 4.55 ; S, 8.23 (%).

Found : C, 43.02 ; H, 5.01 ; N, 14.51 ; Cl, 4.54 ; S, 8.27 (%).

quaternary salt ester :

$^1\text{H-NMR}$ ($\text{d}_6\text{-DMSO}$) δ : 0.90(3H, t, J = 7.2 Hz), 1.36(9H, brs), 1.45(9H, s), 1.85(2H, quintet-like), 2.03(2H, quintet-like), 2.78(3H, brs), 3.18(2H, t, J = 6.9 Hz), 3.28 and 3.34(2H, ABq, J = 15.9 Hz), 3.75(3H, s), 4.43(2H, t, J = 6.9 Hz), 4.71(1H, t, J = 6.6 Hz),

5.18(1H, d, J = 4.8 Hz), 5.21 and 5.30(2H, ABq, J = 11.7 Hz), 5.66 and 5.72(2H, ABq, J = 15.6 Hz), 5.99(1H, dd, J = 4.8 and 9.0 Hz), 6.84(1H, s), 6.88(2H, d, J = 8.7 Hz), 6.97(1H, d, J = 3.6 Hz), 7.20-7.44(12H, m), 7.76(1H, dd, J = 6.3 and 8.1 Hz), 8.42(1H, d, J = 3.6 Hz), 8.60(1H, d, J = 6.3 Hz), 8.88(1H, d, J = 8.1 Hz), 9.69(1H, d, J = 9.0 Hz), 12.1(1H, brs).

IR (KBr) cm^{-1} : 3414, 3062, 3032, 2975, 2935, 1791, 1717, 1686, 1630, 1613, 1585, 1550, 1515, 1495, 1455, 1393, 1367, 1248, 1154, 1018.

MS(ESI): 924⁺(M+H⁺).

3-chloromethyl compound:

¹H-NMR (CDCl₃) δ : 1.08(3H, t, J = 7.2 Hz), 1.53(9H, s), 1.90-2.10(2H, m), 3.26 and 3.50(2H, ABq, J = 18.3 Hz), 3.82(3H, s), 4.40 and 4.56(2H, ABq, J = 11.7 Hz), 4.91(1H, dd, J = 5.1 and 9.0 Hz), 4.99(1H, d, J = 5.1 Hz), 5.21 and 5.28(2H, ABq, J = 11.7 Hz), 5.98(1H, dd, J = 5.1 and 9.6 Hz), 6.91(2H, d, J = 8.7 Hz), 6.93(1H, s), 7.25-7.32(10H, m), 7.36(2H, d, J = 8.7 Hz), 7.72(1H, d, J = 9.6 Hz), 8.01(1H, brs).

IR (KBr) cm^{-1} : 3378, 3291, 3063, 3032, 2975, 2935, 1791, 1721, 1613, 1550, 1515, 1455, 1384, 1368, 1301, 1246, 1155, 1109, 1058, 1032, 1003.

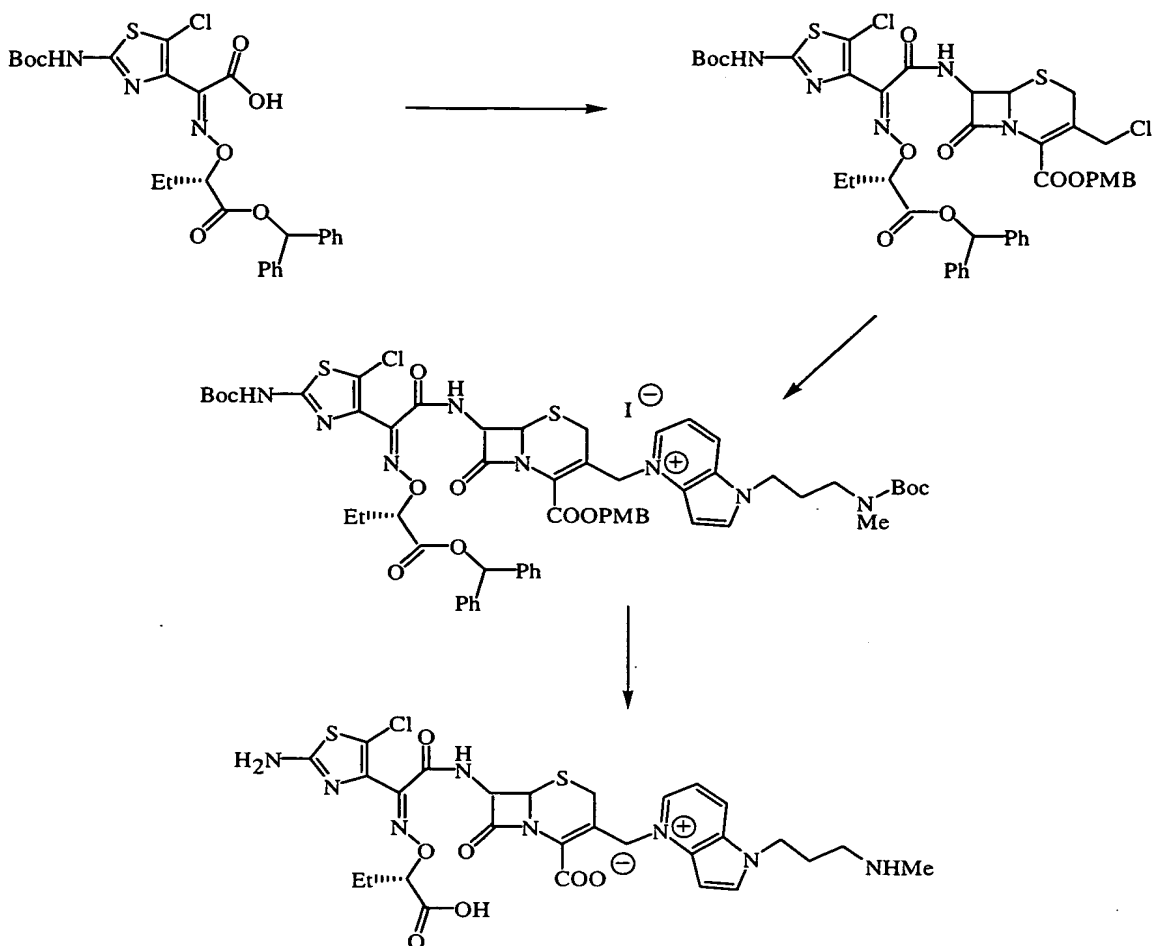
7-side chain

¹H-NMR (d₆-DMSO) δ : 0.89(3H, t, J = 7.5 Hz), 1.46(9H, s), 1.78(2H, quintet like), 4.52(1H, t, J = 6.9 Hz), 6.84(1H, s), 7.23-7.46(10H, m), 12.0(1H, brs).

IR (KBr) cm^{-1} : 3428, 3164, 3063, 3032, 2978, 2936, 1717, 1623, 1557, 1496, 1455, 1392, 1370, 1292, 1251, 1210, 1157, 1105, 1056, 1036.

MS(ESI): 574⁺(M+H⁺).

Example 11



I-3h-5d :

- 5 $^1\text{H-NMR}$ (D_2O) δ : 0.93(3H, t, $J = 7.5$ Hz), 1.83(2H, quintet-like), 2.30(2H, quintet-like), 2.69(3H, s), 3.05(2H, t, $J = 8.1$ Hz), 3.16 and 3.37 (2H, ABq, $J = 17.7$ Hz), 4.52(1H, t, $J = 6.0$ Hz), 4.52(2H, t, $J = 6.3$ Hz), 5.17(1H, d, $J = 4.8$ Hz), 5.55 and 5.68(2H, ABq, $J = 15.0$ Hz), 5.85(1H, d, $J = 4.8$ Hz), 7.03(1H, d, $J = 3.6$ Hz), 7.69(1H, dd, $J = 6.0$ and 8.4 Hz), 8.12(1H, d, $J = 3.6$ Hz), 8.58(1H, d, $J = 8.4$ Hz), 8.64(1H, d, $J = 6.0$ Hz).
- 10 IR (KBr) cm^{-1} : 3388, 2970, 1775, 1602, 1539, 1498, 1463, 1392, 1362, 1316, 1160, 1121, 1061, 1032.
- MS(ESI): 691 $^+$ ($\text{M}+\text{H}^+$).
- Elemental analysis as $\text{C}_{28}\text{H}_{31}\text{ClN}_8\text{O}_7\text{S}_2 \cdot 5.6 \text{ H}_2\text{O}$.
- Calc. : C, 42.46 ; H, 5.37 ; N, 14.15 ; Cl, 4.48 ; S, 8.10 (%).
- 15 Found : C, 42.38 ; H, 5.02 ; N, 14.25 ; Cl, 4.41 ; S, 8.02 (%).

quaternary salt ester :

¹H-NMR (d₆-DMSO) δ : 0.86(3H, t, J = 7.2 Hz), 1.36(9H, brs), 1.46(9H, s), 1.83(2H, quintet-like), 2.03(2H, quintet-like), 2.77(3H, brs), 3.18(2H, t, J = 6.9 Hz), 3.29 and 3.39(2H, ABq, J = 18.9 Hz), 3.76(3H, s), 4.43(2H, t, J = 6.6 Hz), 4.73(1H, t, J = 6.6 Hz), 5.19(1H, d, J = 4.8 Hz), 5.21 and 5.30(2H, ABq, J = 11.7 Hz), 5.70(2H, brs), 5.98(1H, dd, J = 4.8 and 8.7 Hz), 6.84(1H, s), 6.89(2H, d, J = 9.0 Hz), 6.96(1H, d, J = 3.0 Hz), 7.20-7.44(12H, m), 7.78(1H, dd, J = 6.3 and 8.4 Hz), 8.42(1H, d, J = 3.0 Hz), 8.60(1H, d, J = 6.3 Hz), 8.88(1H, d, J = 8.4 Hz), 9.74(1H, d, J = 8.7 Hz), 12.1(1H, brs).

IR (KBr) cm⁻¹: 3423, 3061, 3032, 2974, 2934, 1791, 1718, 1686, 1630, 1613, 1585, 1549, 1515, 1495, 1455, 1392, 1367, 1247, 1154, 1123, 1060, 1029.

MS(ESI): 1177⁺(C₅₉H₆₆ClN₈O₁₂S₂⁺).

3-chloromethyl compound:

¹H-NMR (CDCl₃) δ : 1.02(3H, t, J = 7.2 Hz), 1.53(9H, s), 1.96-2.08(2H, m), 3.40 and 3.59(2H, ABq, J = 18.0 Hz), 3.81(3H, s), 4.43 and 4.58(2H, ABq, J = 11.7 Hz), 4.93(1H, t, J = 6.3 Hz), 4.99(1H, d, J = 5.1 Hz), 5.20 and 5.28(2H, ABq, J = 11.7 Hz), 6.01(1H, dd, J = 5.1 and 9.0 Hz), 6.90(2H, d, J = 9.0 Hz), 6.95(1H, s), 7.25-7.31(10H, m), 7.35(2H, d, J = 9.0 Hz), 7.91(1H, d, J = 9.0 Hz), 7.93(1H, brs).

IR (KBr) cm⁻¹: 3283, 3063, 3031, 2976, 2936, 2836, 1791, 1721, 1613, 1550, 1515, 1455, 1384, 1369, 1301, 1246, 1155, 1058, 1033, 1004.

MS(ESI): 924⁺(M+H⁺).

Elemental analysis as C₄₃H₄₃Cl₂N₅O₁₀S₂ · 0.3 CHCl₃ · 0.8 H₂O.

Calc. : C, 53.33 ; H, 4.64 ; N, 7.18 ; S, 6.58 ; Cl, 10.54 (%).

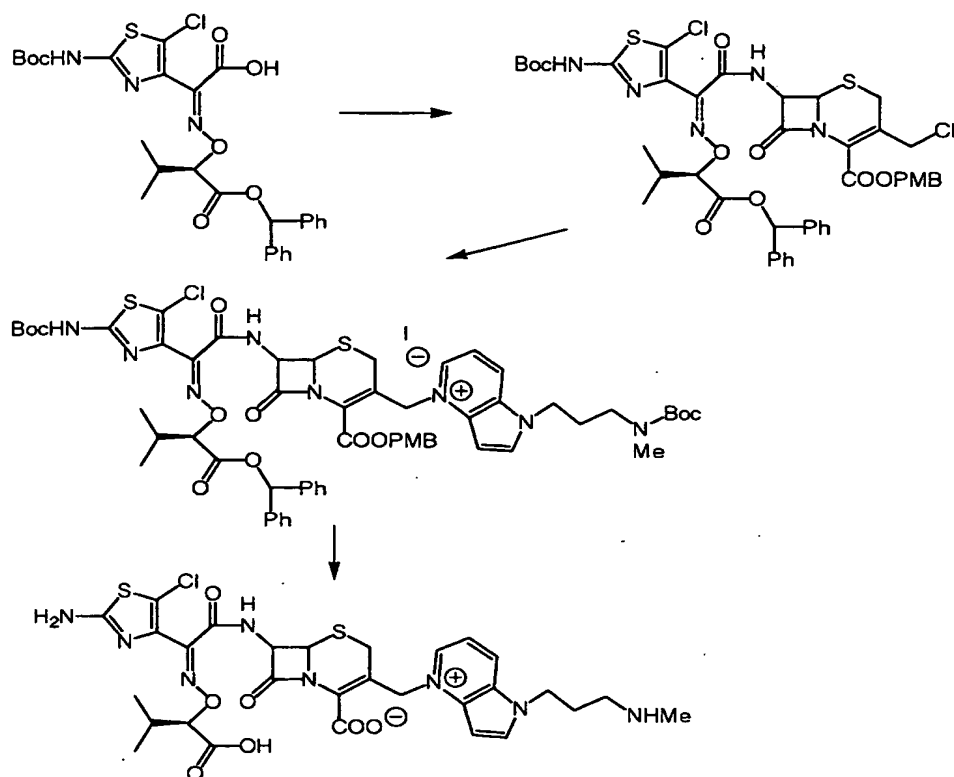
7-side chain

¹H-NMR (d₆-DMSO) δ : 0.89(3H, t, J = 7.5 Hz), 1.46(9H, s), 1.78(2H, quintet like), 4.52(1H, t, J = 6.9 Hz), 6.84(1H, s), 7.23-7.46(10H, m), 12.0(1H, brs).

IR (KBr) cm⁻¹: 3431, 3180, 3064, 3033, 2978, 2934, 1736, 1715, 1621, 1557, 1496, 1455, 1391, 1370, 1295, 1250, 1211, 1158, 1118, 1064, 1034.

MS(ESI): 574⁺(M+H⁺).

Example 12



I-3i-5d :

$^1\text{H-NMR}$ (D_2O) δ : 0.93(6H, d, $J = 6.9$ Hz), 2.09(1H, sextet-like), 2.31(2H, quintet-like), 2.68(3H, s), 3.04(2H, t, $J = 8.1$ Hz), 3.13 and 3.39 (2H, ABq, $J = 17.7$ Hz), 4.27(1H, d, $J = 6.0$ Hz), 4.53(2H, t, $J = 6.9$ Hz), 5.19(1H, d, $J = 4.8$ Hz), 5.58 and 5.66(2H, ABq, $J = 15.0$ Hz), 5.80(1H, d, $J = 4.8$ Hz), 7.07(1H, d, $J = 3.3$ Hz), 7.69(1H, dd, $J = 6.3$ and 8.7 Hz), 8.12(1H, d, $J = 3.3$ Hz), 8.60(1H, d, $J = 8.7$ Hz), 8.65(1H, d, $J = 6.3$ Hz).

IR (KBr) cm^{-1} : 3396, 2965, 1775, 1604, 1538, 1498, 1466, 1391, 1364, 1223, 1121, 1062, 1027.

MS(ESI): 705 $^+$ (M+H $^+$).

Elemental analysis as $\text{C}_{29}\text{H}_{33}\text{ClN}_8\text{O}_7\text{S}_2 \cdot 4.28 \text{ H}_2\text{O}$.

Calc. : C, 44.52 ; H, 5.35 ; N, 14.32 ; Cl, 4.53 ; S, 8.20 (%).

Found : C, 44.14 ; H, 4.96 ; N, 14.38 ; Cl, 4.53 ; S, 8.14 (%).

quarternary ammonium salt ester :

$^1\text{H-NMR}$ ($\text{d}_6\text{-DMSO}$) δ : 0.88(3H, d, $J = 6.9$ Hz), 0.90(3H, d, $J = 6.6$ Hz), 1.36(9H, brs), 1.45(9H, s), 2.02(2H, quintet-like), 2.15(1H, sextet-like), 2.77(3H, brs), 3.17(2H, t, $J = 6.9$ Hz), 3.26 and 3.40(2H, ABq, $J = 18.3$ Hz), 3.75(3H, s), 4.42(2H, t-like), 4.50(1H, t, $J = 6.3$ Hz), 5.18(1H, d, $J = 5.1$ Hz), 5.20 and 5.30(2H, ABq, $J = 11.7$ Hz), 5.65 and 5.71(2H, ABq, $J = 15.6$ Hz), 6.00(1H, dd, $J = 5.1$ and 8.4 Hz), 6.86(1H, s), 6.87(2H, d, $J =$

8.4 Hz), 6.97(1H, d, J = 3.3 Hz), 7.20-7.45(12H, m), 7.75(1H, dd, J = 6.0 and 7.8 Hz), 8.41(1H, d, J = 3.3 Hz), 8.58(1H, d, J = 6.0 Hz), 8.87(1H, d, J = 7.8 Hz), 9.72(1H, d, J = 8.4 Hz), 12.1(1H, brs).

IR (KBr) cm^{-1} : 3393, 3061, 3031, 2972, 2933, 1791, 1719, 1686, 1630, 1613, 1550, 1515,
5 1495, 1455, 1392, 1367, 1248, 1175, 1155, 1125, 1029.

3-chloromethyl compound:

$^1\text{H-NMR}$ (CDCl_3) δ : 0.99(3H, d, J = 7.2 Hz), 1.02(3H, d, J = 7.2 Hz), 1.53(9H, s),
2.37(1H, sextet-like), 3.35 and 3.55(2H, ABq, J = 18.3 Hz), 3.82(3H, s), 4.42 and
4.54(2H, ABq, J = 12.0 Hz), 4.76(1H, d, J = 6.0 Hz), 4.99(1H, d, J = 5.1 Hz), 5.21 and
10 5.28(2H, ABq, J = 11.7 Hz), 5.95(1H, dd, J = 5.1 and 9.3 Hz), 6.91(2H, d, J = 8.7 Hz),
6.94(1H, s), 7.25-7.32(10H, m), 7.36(2H, d, J = 8.7 Hz), 7.51(1H, d, J = 9.3 Hz), 8.03(1H,
brs).

IR (KBr) cm^{-1} : 3292, 3063, 3031, 2970, 2935, 2876, 2836, 1792, 1722, 1613, 1550, 1515,
1454, 1387, 1369, 1333, 1302, 1247, 1155, 1096, 1031.

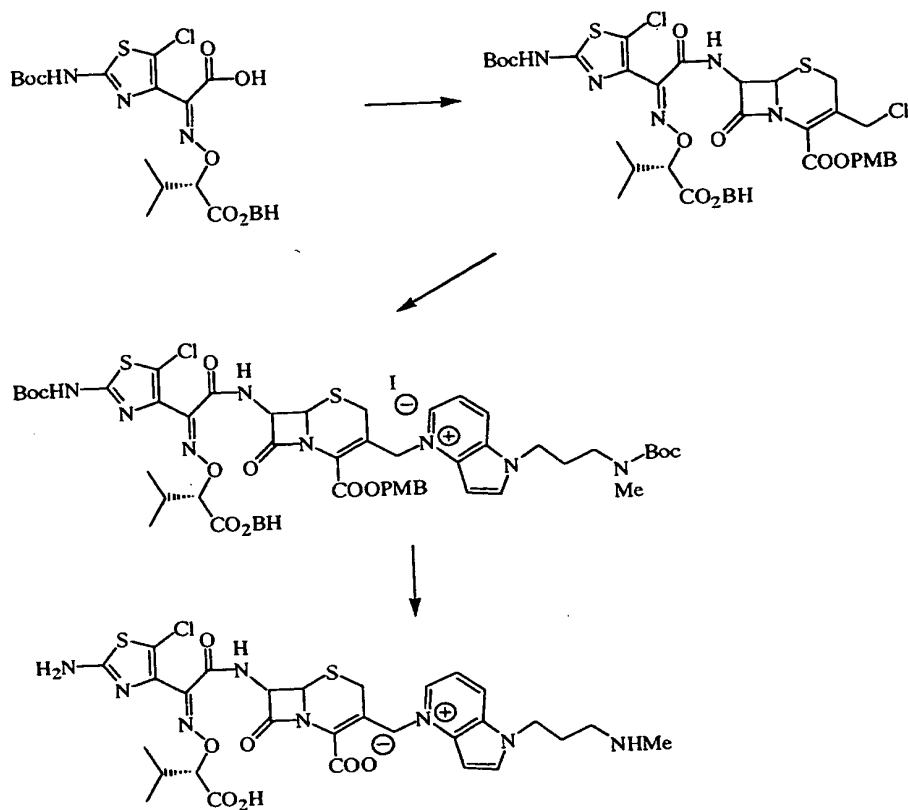
15 MS(ESI): 938 $^+$ (M+H $^+$).

7-side chain

$^1\text{H-NMR}$ ($\text{D}_6\text{-DMSO}$) δ : 0.83(3H, d, J = 6.9 Hz), 0.93(3H, d, J = 6.6 Hz), 1.46(9H, s),
2.05(1H, sex., J = ca 6.9 Hz), 4.28(1H, d, J = 7.2 Hz), 6.86(1H, s), 7.24-7.31(6H, m),
7.43-7.45(4H, m).

20 IR(KBr) cm^{-1} : 3431, 2971, 2934, 1740, 1715, 1619, 1555, 1371, 1251, 1157, 1034, 699.

Example 13



1-3j-5d :

¹H-NMR (D₂O) δ : 0.94(3H, d, J = 7.2 Hz), 0.98(3H, d, J = 6.9 Hz), 2.13(1H, sextet-like), 2.31(2H, quintet-like), 2.68(3H, s), 2.91(2H, t, J = 7.8 Hz), 3.15 and 3.37 (2H, ABq, J = 17.7 Hz), 4.35(1H, d, J = 5.4 Hz), 4.52(2H, t, J = 6.9 Hz), 5.17(1H, d, J = 4.8 Hz), 5.55 and 5.67(2H, ABq, J = 15.3 Hz), 5.87(1H, d, J = 4.8 Hz), 7.04(1H, d, J = 3.3 Hz), 7.69(1H, dd, J = 6.0 and 8.1 Hz), 8.12(1H, d, J = 3.3 Hz), 8.59(1H, d, J = 8.1 Hz), 8.64(1H, d, J = 6.0 Hz).

IR (KBr) cm⁻¹: 3389, 2965, 1777, 1601, 1539, 1498, 1466, 1391, 1364, 1223, 1120, 1062, 1019.

MS(ESI): 705⁺(M+H⁺).

Elemental analysis as C₂₉H₃₃ClN₈O₇S₂ · 6.5 H₂O.

Calc. : C, 42.36 ; H, 5.64 ; N, 13.63 ; Cl, 4.31 ; S, 7.80 (%).

Found : C, 42.01 ; H, 4.82 ; N, 13.51 ; Cl, 4.26 ; S, 7.89 (%).

7-side chain

¹H-NMR (d₆-DMSO) δ : 0.85(3H, d, J = 6.6 Hz), 0.93(3H, d, J = 6.6 Hz), 1.46(9H, s),

2.07(1H, sextet-like), 4.35(1H, d, J = 7.2 Hz), 6.87(1H, s), 7.1-7.5(11H, m), 12.0(1H, brs).

IR (KBr) cm^{-1} : 3422, 3207, 3064, 3032, 2976, 2933, 2876, 1717, 1629, 1555, 1495, 1455, 1393, 1370, 1295, 1248, 1156, 1055, 1032.

5 MS(ESI): 588⁺(M+H⁺).

Elemental analysis as $\text{C}_{28}\text{H}_{30}\text{ClN}_8\text{O}_7\text{S}_1 \cdot 1.04 \text{H}_2\text{O} \cdot 0.12 \text{AcOEt}$.

Calc. : C, 55.41 ; H, 5.39 ; N, 6.81 ; Cl, 5.74 ; S, 5.19 (%).

Found : C, 55.44 ; H, 5.11 ; N, 7.20 ; Cl, 5.67 ; S, 4.80 (%).

3-chloromethyl compound:

10 ¹H-NMR (CDCl_3) δ : 0.95(3H, d, J = 7.2 Hz), 1.04(3H, d, J = 6.9 Hz), 1.53(9H, s), 2.35(1H, m), 3.43 and 3.59(2H, ABq, J = 18.3 Hz), 3.81(3H, s), 4.45 and 4.57(2H, ABq, J = 11.7 Hz), 4.84(1H, d, J = 4.5 Hz), 4.99(1H, d, J = 4.8 Hz), 5.21 and 5.28(2H, ABq, J = 12.0 Hz), 5.99(1H, dd, J = 4.8 and 9.0 Hz), 6.91(2H, d, J = 8.7 Hz), 6.98(1H, s), 7.25-7.32(10H, m), 7.35(2H, d, J = 8.7 Hz), 7.92(1H, s), 7.99(1H, d, J = 9.0 Hz).

15 IR (KBr) cm^{-1} : 3392, 3283, 3062, 3032, 2969, 2934, 2835, 1791, 1721, 1613, 1585, 1551, 1514, 1455, 1387, 1368, 1302, 1246, 1155, 1096, 1061, 1030.

MS(ESI): 938⁺(M+H⁺).

Elemental analysis as $\text{C}_{44}\text{H}_{45}\text{Cl}_2\text{N}_5\text{O}_{10}\text{S}_2 \cdot 0.1 \text{CHCl}_3 \cdot 0.4 \text{H}_2\text{O} \cdot 0.4 \text{AcOEt}$.

Calc. : C, 55.26 ; H, 4.98 ; N, 7.05 ; S, 6.46 ; Cl, 8.21 (%).

20 Found : C, 55.22 ; H, 4.64 ; N, 6.90 ; S, 6.20 ; Cl, 8.37 (%).

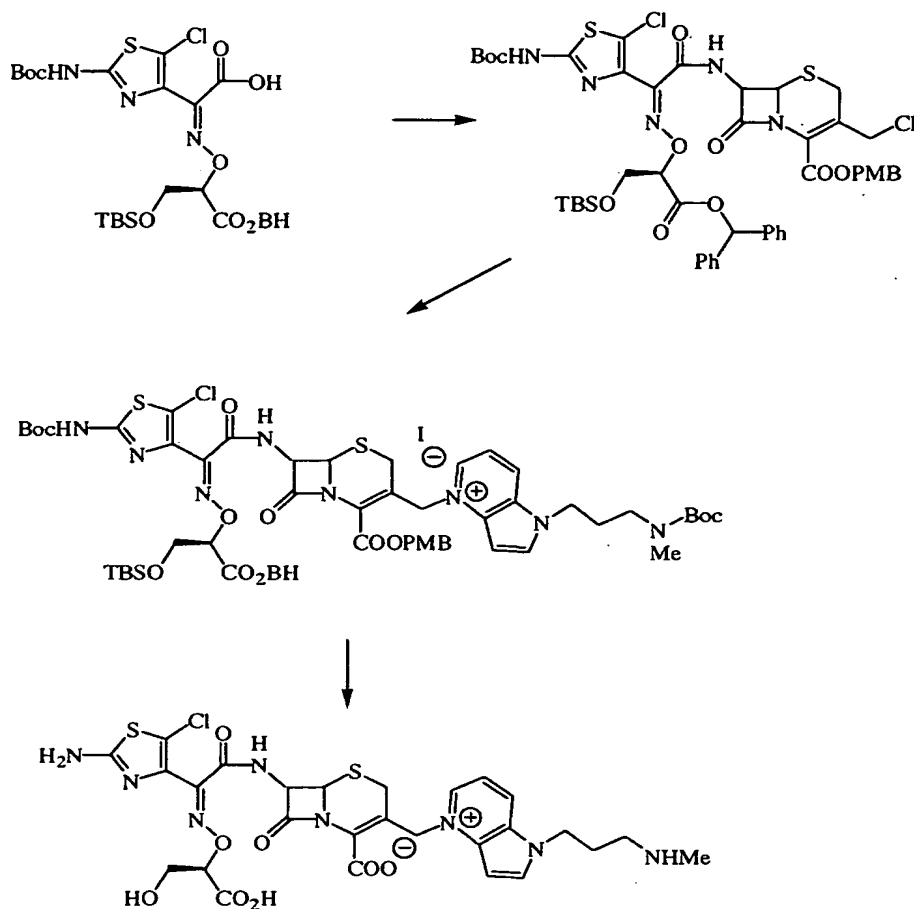
quarternary ammonium salt ester :

¹H-NMR (d_6 -DMSO) δ : 0.87(3H, d, J = 6.9 Hz), 0.89(3H, d, J = 7.2 Hz), 1.36(9H, brs), 1.46(9H, s), 2.03(2H, quintet-like), 2.15(1H, sextet-like), 2.78(3H, brs), 3.18(2H, t-like), 3.27 and 3.43(2H, ABq, J = 13.2 Hz), 3.76(3H, s), 4.43(2H, t-like), 4.56(1H, d, J = 6.0 Hz), 5.20(1H, d, J = 5.4 Hz), 5.21 and 5.30(2H, ABq, J = 11.7 Hz), 5.70(2H, brs), 6.00(1H, dd, J = 5.4 and 8.4 Hz), 6.86(1H, s), 6.89(2H, d, J = 8.7 Hz), 6.95(1H, d, J = 3.3 Hz), 7.21-7.44(12H, m), 7.78(1H, dd, J = 6.3 and 8.4 Hz), 8.41(1H, d, J = 3.3 Hz), 8.60(1H, d, J = 6.3 Hz), 8.87(1H, d, J = 8.4 Hz), 9.74(1H, d, J = 8.4 Hz), 12.1(1H, brs).

25 IR (KBr) cm^{-1} : 3423, 3061, 3032, 2972, 2933, 1792, 1718, 1685, 1630, 1613, 1584, 1550, 1515, 1495, 1455, 1392, 1367, 1247, 1154, 1061, 1028.

30 MS(ESI): 1191⁺(M-I⁺).

Example 14



I-3k-5d :

$^1\text{H-NMR}$ (D_2O) δ : 2.31(2H, quintet-like), 2.68(3H, s), 3.05(2H, t, $J = 8.1$ Hz), 3.14 and 3.40 (2H, ABq, $J = 18.0$ Hz), 3.91(2H, m), 4.53(2H, t, $J = 6.9$ Hz), 4.69(1H, m), 5.20(1H, d, $J = 4.8$ Hz), 5.58 and 5.67(2H, ABq, $J = 14.7$ Hz), 5.84(1H, d, $J = 4.8$ Hz), 7.06(1H, d, $J = 3.6$ Hz), 7.69(1H, dd, $J = 6.3$ and 8.4 Hz), 8.12(1H, d, $J = 3.6$ Hz), 8.60(1H, d, $J = 8.4$ Hz), 8.65(1H, d, $J = 6.3$ Hz).

IR (KBr) cm^{-1} : 3388, 1772, 1605, 1539, 1498, 1466, 1391, 1362, 1321, 1223, 1152, 1120, 1064, 1034.

MS(ESI): 693 $^+$ (M+H $^+$).

Elemental analysis as $\text{C}_{27}\text{H}_{29}\text{ClN}_8\text{O}_8\text{S}_2 \cdot 5.62 \text{ H}_2\text{O}$.

Calc. : C, 40.82 ; H, 5.11 ; N, 14.11 ; Cl, 4.46 ; S, 8.07 (%).

Found : C, 40.41 ; H, 4.70 ; N, 14.05 ; Cl, 4.27 ; S, 8.03 (%).

7-side chain

$^1\text{H-NMR}$ ($\text{d}_6\text{-DMSO}$) δ : -0.03(3H, s), -0.01(3H, s), 0.77(9H, s), 1.46(9H, s), 3.86-3.99(2H,

m), 4.62(1H, t-like), 6.83(1H, s), 7.20-7.50(11H, m), 11.1(1H, brs).

IR (KBr) cm^{-1} : 3450, 3159, 3078, 2956, 2795, 1772, 1698, 1428, 1418, 1373, 1294, 1240, 1190, 1002.

MS(ESI): 690⁺(M+H⁺).

5 3-chloromethyl compound:

¹H-NMR (CDCl₃) δ : 0.00(6H, s), 0.82(9H, s), 1.49(9H, s), 3.21 and 3.46(2H, ABq, J = 18.0 Hz), 3.77(3H, s), 4.12(2H, t-like), 4.36 and 4.52(2H, ABq, J = 12.0 Hz), 4.93(1H, d, J = 4.8 Hz), 5.04(1H, m), 5.16 and 5.24(2H, ABq, J = 11.7 Hz), 5.93(1H, dd, J = 4.8 and 9.3 Hz), 6.85(2H, d, J = 8.7 Hz), 6.89(1H, s), 7.22-7.29(10H, m), 7.32(2H, d, J = 8.7 Hz), ,
10 7.61(1H, d, J = 9.3 Hz), 8.22(1H, s).

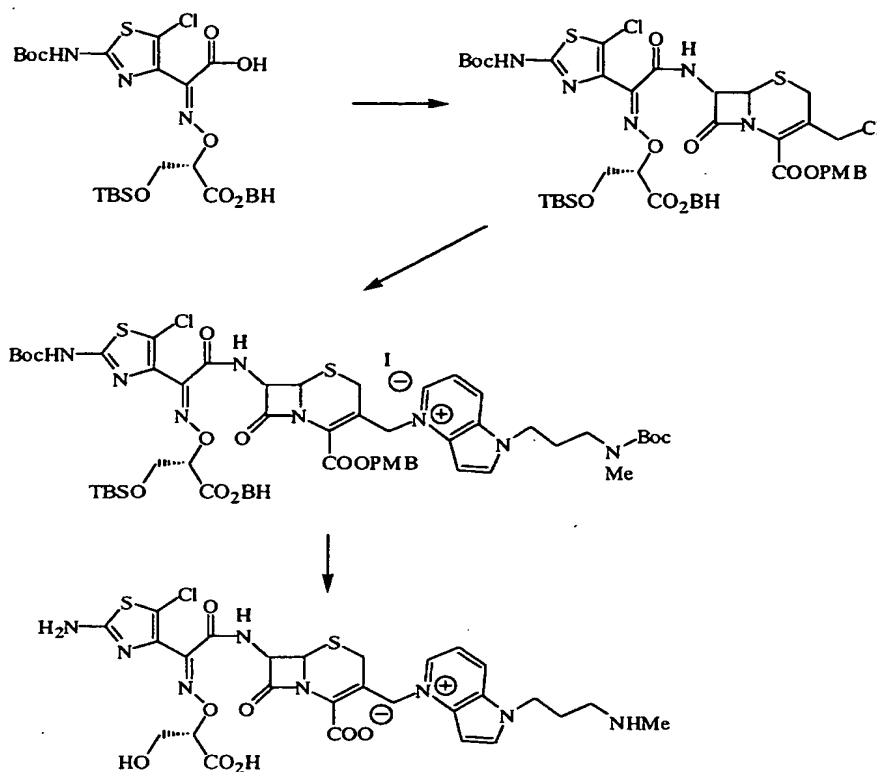
IR (KBr) cm^{-1} : 3470, 3283, 2954, 2932, 1788, 1720, 1612, 1585, 1556, 1514, 1455, 1388, 1368, 1301, 1248, 1173, 1157, 1102, 1064, 1034.

quarternary ammonium salt ester :

IR (KBr) cm^{-1} : 3421, 3062, 3032, 2930, 2855, 1791, 1718, 1686, 1630, 1612, 1585, 1550,
15 1515, 1495, 1455, 1392, 1367, 1248, 1175, 1154, 1102, 1064, 1029.

MS(ESI): 1293⁺(M-I⁺).

Example 15



I-3l-5d :

¹H-NMR (D₂O) δ : 2.31(2H, quintet-like), 2.68(3H, s), 3.05(2H, t, J = 8.1 Hz), 3.17 and 3.38 (2H, ABq, J = 17.7 Hz), 3.94(2H, m), 4.53(2H, t, J = 7.2 Hz), 4.70(1H, m), 5.18(1H, d, J = 4.8 Hz), 5.55 and 5.68(2H, ABq, J = 15.0 Hz), 5.88(1H, d, J = 4.8 Hz), 7.04(1H, d, J = 3.3 Hz), 7.69(1H, dd, J = 6.3 and 8.4 Hz), 8.12(1H, d, J = 3.3 Hz), 8.60(1H, d, J = 8.4 Hz), 8.64(1H, d, J = 6.3 Hz).

IR (KBr) cm⁻¹: 3398, 1774, 1603, 1538, 1498, 1466, 1392, 1362, 1320, 1064.

MS(ESI): 693⁺(M+H⁺).

10 Elemental analysis as C₂₇H₂₉ClN₈O₈S₂ · 9.0 H₂O.

Calc. : C, 37.92 ; H, 5.54 ; N, 13.10 ; Cl, 4.15 ; S, 7.50 (%).

Found : C, 37.77 ; H, 4.42 ; N, 13.09 ; Cl, 4.24 ; S, 7.49 (%).

7-side chain

¹H-NMR (d₆-DMSO) δ : -0.03(3H, s), -0.01(3H, s), 0.77(9H, s), 1.46(9H, s), 3.87-3.99(2H, m), 4.63(1H, t-like), 6.83(1H, s), 7.22-7.48(11H, m), 11.1(1H, brs).

IR (KBr) cm⁻¹: 3450, 3159, 3078, 2955, 2794, 1772, 1697, 1428, 1417, 1373, 1294, 1240, 1191, 1002.

MS(ESI): 690⁺(M+H⁺).

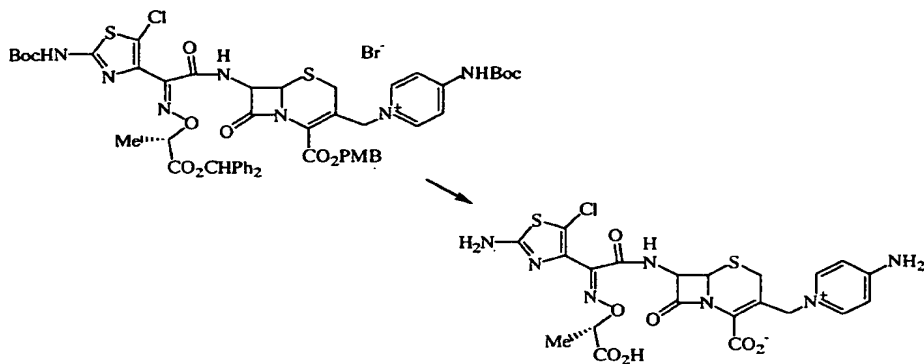
quarternary ammonium salt ester :

IR (KBr) cm^{-1} : 3423, 3062, 3032, 2930, 2855, 1792, 1718, 1687, 1630, 1613, 1585, 1550, 1515, 1495, 1455, 1392, 1367, 1248, 1174, 1154, 1102, 1064, 1030.

MS(ESI): 1293⁺(M-I⁺).

5

Example 16



I-3f-2a :

¹H-NMR (D6-dmso) δ : 1.39(3H, J = 7.2 Hz), 2.99 and 3.44(2H, ABq, J = 17.4 Hz),

10 4.56(1H, q, J = 7.2 Hz), 4.68 and 5.16(2H, ABq, J = 13.2 Hz), 5.05(1H, d, J = 4.8 Hz),
5.71(1H, dd, J = 4.8, 8.4 Hz), 6.83 and 8.46(4H, A2B2q, J = 6.6 Hz), 7.42(2H, s), 8.19(2H,
s), 9.71(1H, d, J = 8.4 Hz).

IR (KBr) cm^{-1} : 3409, 3205, 1776, 1656, 1539, 1375, 1168, 1035, 842 .

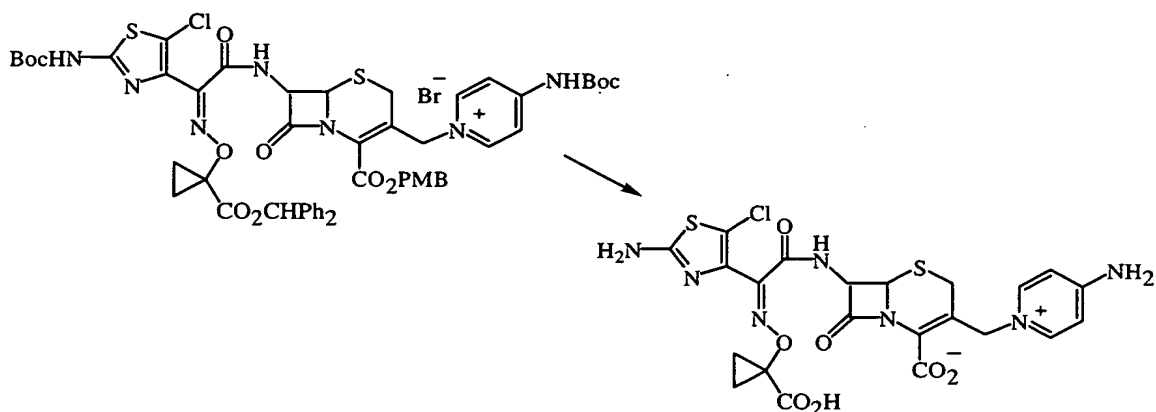
Positive ESIMS: m/z 582 [M+H]⁺ . Negative ESIMS: m/z 580 [M-H]⁻ .

15 quaternary salt ester :

¹H-NMR (CDCl₃-CD₃OD) δ : 1.53(9H, s), 1.56(9H, s), 1.61(3H, d, J = 7.2 Hz), 3.18 and
3.75(2H, ABq, J = 18.6 Hz), 3.83(3H, s), 4.99(1H, q, J = 7.2 Hz), 5.09(1H, d, J = 5.1 Hz),
5.21 and 5.31(2H, ABq, J = 11.7 Hz), 5.27 and 5.47(2H, ABq, J = 13.8 Hz), 5.94(1H, d, J
= 5.1 Hz), 6.90(2H, J = 9 Hz), 6.91 (1H, s), 7.31-7.36(12H, m), 7.96(2H, m), 8.73(1H, d,
20 J = 6.6 Hz) .

IR (KBr) cm^{-1} : 3401, 2978, 2935, 1793, 1741, 1719, 1642, 1587, 1532,
1247, 1148, 1063, 701 .

Example 17



I-3c-2a :

¹H-NMR (D6-dmso) δ : 1.28 -1.36 (4H, m), 3.03 and 3.44(2H, ABq, J = 17.7 Hz), 4.72 and 5.12(2H, ABq, J = 13.8 Hz), 5.05(1H, d, J = 4.8 Hz), 5.71(1H, dd, J = 4.8, 8.7 Hz),
 5 6.85 and 8.40(4H, A2B2q, J = 6.6 Hz), 7.45(2H, s), 8.27(2H, s), 9.71(1H, m).

IR (KBr) cm^{-1} : 3349, 3199, 1776, 1656, 1538, 1376, 1170, 1035, 972 .

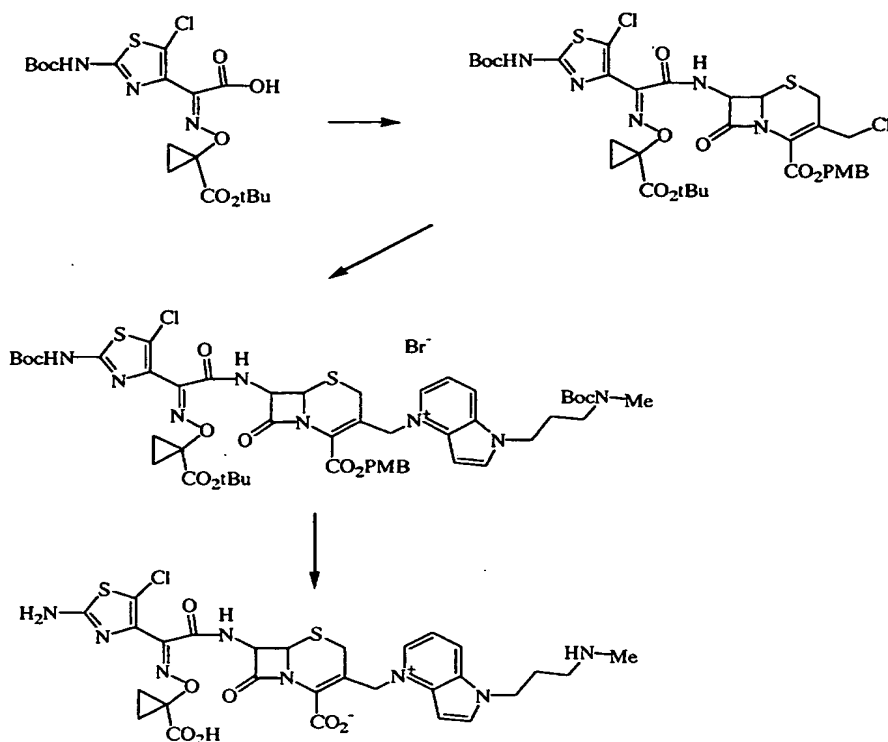
Positive ESIMS: m/z 594 $[M+H]^+$. Negative ESIMS: m/z 592 $[M-H]^-$.

quaternary salt ester :

¹H-NMR (CDCl₃) δ : 1.35(9H, s), 1.41 - 1.54(22H, m), 3.22 and 3.89(2H, ABq, J = 18.3
 10 Hz), 3.83(3H, s), 5.12(1H, d, J = 5.1 Hz), 5.22 and 5.30(2H, ABq, J = 11.7 Hz), 5.48 and 5.64(2H, ABq, J = 8.4 Hz), 6.02(1H, dd, J = 5.1, 9 Hz), 6.91 and 7.34(4H, A2B2q, J = 8.4 Hz), 8.17(1H, br s), 8.38 and 8.93(4H, A2B2q, J = 7.5 Hz), 8.61(1H, d, J = 9 Hz), 10.2(1H, s) .

IR (KBr) cm^{-1} : 3425, 3249, 2979, 2935, 1794, 1718, 1642, 1586, 1532, 1458, 1370, 1247,
 15 1149, 1031, 838 .

Example 18



I-3c-5d :

¹H-NMR (D₂O) δ : 1.26-1.32 (4H, m), 2.31(2H, q like), 2.68(3H, s), 3.06(2H, t, J = 8.1 Hz), 3.15 and 3.39(2H, ABq, J = 17.7 Hz), 4.54(2H, t like), 5.17(1H, d, J = 4.5 Hz), 5.57 and 5.68(2H, ABq, J = 15 Hz), 5.80(1H, d, J = 4.5 Hz), 7.05(1H, d, J = 3.3 Hz), 7.70(1H, t, J = ca 7 Hz), 8.13(1H, d, J = 2.4 Hz), 8.60(1H, d, J = 8.4 Hz), 8.65(1H, d, J = 6 Hz).

IR (KBr) cm⁻¹: 3398, 2820, 1773, 1608, 1540, 1395, 1225, 1033, 968, 761 .

Positive ESIMS: m/z 689 [M+H]⁺ . Negative ESIMS: m/z 687 [M-H]⁻ .

quaternary salt ester :

¹H-NMR (CDCl₃) δ : 1.41(9H, s), 1.46-1.52(22H, m), 2.23(2H, m), 2.92(3H, s), 3.35 and 3.78(2H, ABq, J = 18 Hz), 3.38(2H, m), 3.81(3H, s), 4.45(2H, t like), 5.20(1H, d, J = 5.1 Hz), 5.24 and 5.30(2H, ABq, J = 11.4 Hz), 5.76 and 5.90(2H, ABq, J = 14.1 Hz), 6.02(1H, dd, J = 5.1, 8.7 Hz), 6.87 and 7.33(4H, A2B2q, J = 8.4 Hz), 7.01 (1H, br s), 7.64 (1H, t like), 8.02(1H, br s), 8.30(2H, m), 8.51(2H, d like), 8.61(1H, d, J = 9 Hz) .

IR (KBr) cm⁻¹: 3424, 3253, 2976, 2932, 1793, 1716, 1685, 1632, 1613, 1549, 1516, 1455, 1392, 1367, 1248, 1152, 1031, 754 .

3-Cl methyl compound:

¹H-NMR (CDCl₃) δ : 1.41(9H, s), 1.47-1.53(13H, m), 3.48 and 3.63(2H, ABq, J = 18.3 Hz), 3.82(3H, s), 4.49(2H, s), 5.06(1H, d, J = 5.1 Hz), 5.08(1H, q, J = 7.2 Hz), 5.21 and

5.28(2H, ABq, $J = 11.7$ Hz), 5.99(1H, dd, $J = 5.1, 9.3$ Hz), 6.91 and 7.36(4H, A2B2q, $J = 8.7$ Hz), 8.13(1H, br s), 8.59(1H, d, $J = 9.3$ Hz).

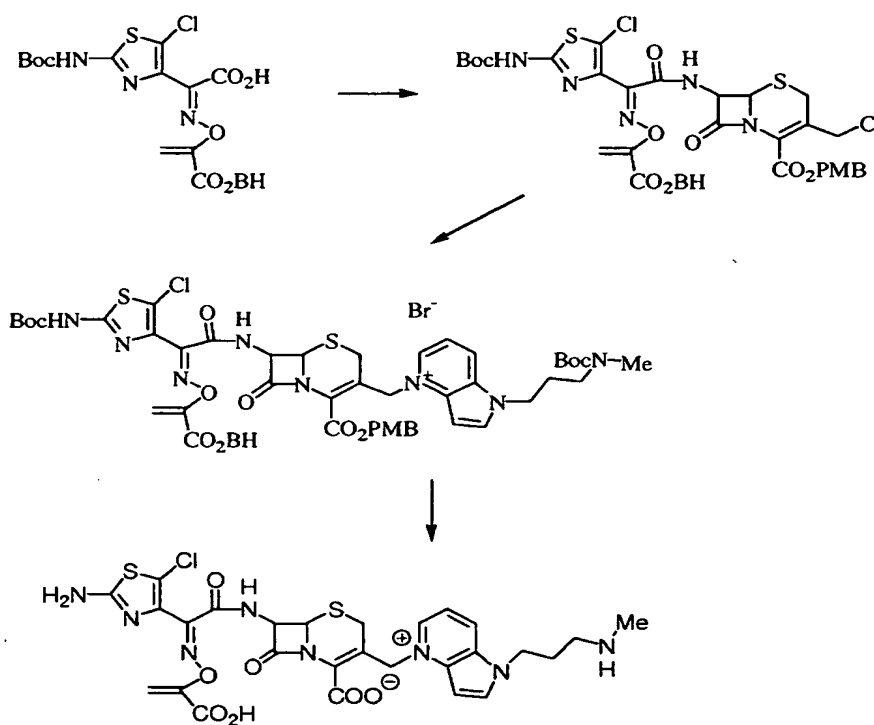
IR (KBr) cm^{-1} : 3378, 3268, 2979, 2935, 2838, 1793, 1719, 1613, 1550, 1517, 1457, 1369, 1248, 1154, 1032.

5 7-side chain

$^1\text{H-NMR}$ (CDCl_3) δ : 1.40(9H, s), 1.43-1.55(13H, m).

IR (CHCl_3) cm^{-1} : 3405, 2983, 2935, 1719, 1626, 1550, 1153.

Example 19



10

I-3b-5d :

$^1\text{H-NMR}$ (D_2O) δ : 2.31(2H, q like, $J = 7.5$ Hz), 2.68(3H, s), 3.04(2H, t like), 3.17 and 3.31(2H, ABq, $J = 17.7$ Hz), 4.53(2H, t like), 5.10(1H, d,

$J = 2.1$ Hz), 5.12(1H, d, $J = 4.5$ Hz), 5.27(1H, d, $J = 2.1$ Hz), 5.51 and

15 5.76(2H, ABq, $J = 15$ Hz), 5.88(1H, d, $J = 4.5$ Hz), 6.99(1H, d, $J = 3.6$),

7.67(1H, dd, $J = 6.4, 8.1$ Hz), 8.12(1H, d, $J = 3.6$ Hz), 8.59(1H, d, $J =$

8.1 Hz), 8.63(1H, d, $J = 6.4$ Hz). IR (KBr) cm^{-1} : 3398, 1774, 1606, 1539, 1498, 1468, 1392, 1203, 759.

Positive ESIMS: m/z 675 $[\text{M}+\text{H}]^+$.

Elemental analysis as $C_{27}H_{27}N_8O_7S_2Cl \cdot 5.5H_2O$.

Calc. : C,41.89; H,4.95; N,14.47; S,8.28; Cl,4.58 (%).

Found : C,41.92; H,4.72; N,14.49; S,8.38; Cl,4.66 (%).

quaternary salt ester :

5 1H -NMR ($CDCl_3$) δ : 1.48(9H, s), 1.53(9H, s), 2.20(2H, m), 2.90(3H, s) 3.19
and 3.64(2H, ABq, J = 18 Hz), 3.36(2H, t like), 3.78(3H, s), 4.42(2H, t
like), 4.95(1H, d, J = 4.8 Hz), 5.20 and 5.28(2H, ABq, J = 11.7 Hz), 5.59(1H, d, J = 1.5
Hz), 5.75(1H, d, J = 1.5 Hz), 5.84(1H, dd, J = 4.8, 8.6 Hz), 6.83 (2H, d, J = 8.7 Hz),
6.89(1H, s), 7.04(1H, br s), 7.23- 7.36 (12H, m), 7.62(1H, m), 8.20(1H, m), 8.46(1H, d, J
10 = 9.3 Hz), 8.56(1H, d, J = 6.0 Hz), 8.65(1H, m) .

IR ($CHCl_3$) cm^{-1} : 3403, 1793, 1720, 1685, 1632, 1613, 1551, 1517, 1154 .

3-chloromethyl compound:

1H -NMR ($CDCl_3$) δ : 1.53(9H, s), 3.23 and 3.43(2H, ABq, J = 18 Hz), 3.80(3H, s), 4.36
and 4.55(2H, ABq, J = 12 Hz), 4.75(1H, d, J = 5.1 Hz), 5.16
15 and 5.25(2H, ABq, J = 11.4 Hz), 5.61(1H, d, J = 1.8), 5.81(1H, d, J = 1.8), 5.88(1H, dd, J =
5.1, 9.0 Hz), 6.87- 6.92 (3H, m), 7.16 -7.39 (12H, m), 8.56(1H, br s).

IR ($CHCl_3$) cm^{-1} : 3403, 1793, 1725, 1613, 1550, 1517, 1248, 1215, 1155.

7-side chain :

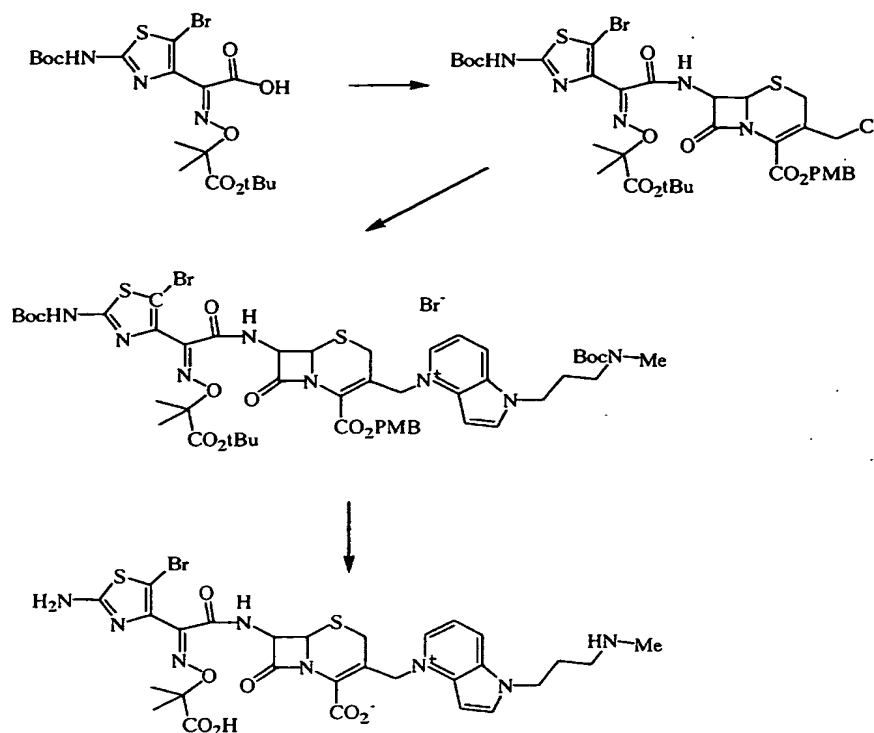
1H -NMR ($CDCl_3$) δ : 1.48(9H, s), 5.65(1H, d, J = 2.4), 5.75(1H, d, J = 2.4), 6.93(1H,
20 s), 7.27 -7.34(10H, m).

Positive FABMS(Matrix:m-NBA): m/z 558[M+H]⁺, 580[M+Na]⁺, 1115[2M+ H]⁺ .

Negative FABMS(Matrix:m-NBA): m/z 556[M-H]⁻, 1113[2M H]⁻ .

IR ($CHCl_3$) cm^{-1} : 3602, 3404, 1723, 1603, 1550, 1285, 1253, 1227, 1155 .

25 Example 20



I-4d-5d :

$^1\text{H-NMR}$ (D_2O) δ : 1.47 (6H, s), 2.30(2H, q like), 2.68(3H, s), 3.06(2H, t, $J = 8$ Hz), 3.18 and 3.39(2H, ABq, $J = 17.7$ Hz), 4.52(2H, t like), 5.18(1H, d, $J = 4.8$ Hz), 5.56 and 5.68(2H, ABq, $J = 15$ Hz), 5.82(1H, d, $J = 4.8$ Hz), 7.04(1H, d, $J = 3.3$ Hz), 7.68(1H, t like), 8.12(1H, d, $J = 3.6$ Hz), 8.58(1H, d, $J = 8.1$ Hz), 8.64(1H, d, $J = 6$ Hz).

IR (KBr) cm^{-1} : 3405, 1772, 1608, 1535, 1394, 1362, 1160, 790, 760 .

Positive ESIMS: m/z 735 $[\text{M}+\text{H}]^+$. Negative ESIMS: m/z 733 $[\text{M}-\text{H}]^-$.

Elemental analysis $\text{C}_{28}\text{H}_{31}\text{N}_8\text{O}_7\text{S}_2\text{Br} \cdot 5\text{H}_2\text{O}$ として.

Calc. : C,40.73; H,5.00; N,13.57; S,7.77; Br,9.68 (%).

Found : C,40.67; H,4.91; N,13.39; S,7.50; Br,9.64 (%).

quaternary salt ester :

$^1\text{H-NMR}$ (CDCl_3) δ : 1.43(9H, s), 1.48(9H, s), 1.51(3H, s), 1.59(3H, s), 2.22(2H, m), 2.91(3H, s), 3.37(2H, t like), 3.31 and 3.80(2H, ABq, $J = 18.6$ Hz), 3.82(3H, s), 4.45(2H, t like), 5.19(1H, d, $J = 5.4$ Hz), 5.23 and 5.30(2H, ABq, $J = 11.4$ Hz), 5.64 and 5.79(2H, ABq, $J = 15$ Hz), 6.07(1H, dd, $J = 5.4, 9$ Hz), 6.87 and 7.33(4H, A2B2q, $J = 8.7$ Hz), 7.04 (1H, br s), 7.67(1H, t like), 8.06 (1H, d, $J = 9$ Hz), 8.26(1H, br s), 8.39(1H, br s), 8.52(1H, d, $J = 9$ Hz), 8.58(1H, d, $J = 6$ Hz) .

3-chloromethyl compound:

$^1\text{H-NMR}$ (CDCl_3) δ : 1.43(9H, s), 1.52(9H, s), 1.62(6H, s), 3.48 and 3.65(2H, ABq, J = 18.3 Hz), 3.82(3H, s), 4.44 and 4.55(2H, ABq, J = 12 Hz), 5.04(1H, d, J = 4.8 Hz), 5.19 and 5.27(2H, ABq, J = 12 Hz), 6.03(1H, dd, J = 5.1, 9 Hz), 6.91 and 7.35(4H, A2B2q, J = 8.7 Hz), 8.02(1H, d, J = 9 Hz), 8.17(1H, br s).

5 IR (KBr) cm^{-1} : 3280, 2980, 2935, 2837, 1789, 1720, 1614, 1549, 1516, 1369, 1248, 1155 .

7-side chain:

$^1\text{H-NMR}$ (CDCl_3) δ : 1.48(9H, s), 1.49(9H, s), 1.53(3H, s), 1.56(3H, s) .

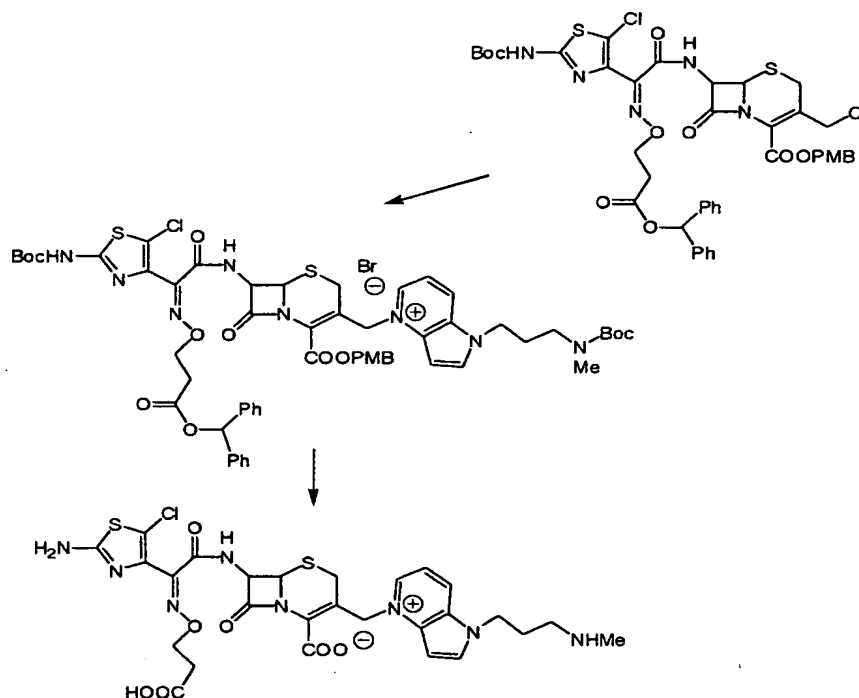
IR (CHCl_3) cm^{-1} : 3406, 3019, 2983, 2937, 1724, 1544, 1369, 1226, 1151 .

10 Positive ESIMS: m/z 508 $[\text{M}+\text{H}]^+$, m/z 530 $[\text{M}+\text{Na}]^+$.

Negative ESIMS: m/z 506 $[\text{M}-\text{H}]^-$, m/z 528 $[\text{M}+\text{Na}-2\text{H}]^-$.

The other example compounds are shown below.

Example 22



15

$^1\text{H-NMR}$ (D_2O) δ : 2.31(2H, m), 2.59(2H, t, J = 6.9 Hz), 2.69(3H, s), 3.06(2H, m), 3.21 and 3.35 (2H, ABq, J = 17.7 Hz), 4.39(2H, m), 4.53(2H, t, J = 6.9 Hz), 5.14(1H, d, J = 5.1 Hz), 5.54 and 5.71(2H, ABq, J = 15.0 Hz), 5.76(1H, d, J = 5.1 Hz), 7.03(1H, d, J = 3.3 Hz), 7.69(1H, dd, J = 6.3 and 8.4 Hz), 8.13(1H, d, J = 3.3 Hz), 8.60(1H, d, J = 8.4 Hz),

20 8.66(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1} : 3397, 3132, 2458, 1775, 1615, 1540, 1499, 1466, 1389, 1223, 1164, 1122, 1063, 1027.

MS(ESI): 677⁺(M+H⁺).

Elemental analysis as $\text{C}_{27}\text{H}_{29}\text{ClN}_8\text{O}_7\text{S}_2 \cdot 2.8 \text{ H}_2\text{O}$.

5 Calc. : C, 44.57 ; H, 4.79 ; N, 15.40 ; Cl, 4.87 ; S, 8.81 (%).

Found : C, 44.51 ; H, 4.57 ; N, 15.37 ; Cl, 4.81 ; S, 8.66 (%).

3-chloromethyl compound:

¹H-NMR (CDCl_3) δ : 1.52(9H, s), 2.89(2H, m), 3.28 and 3.53(2H, ABq, J = 18.3 Hz),
3.81(3H, s), 4.22 and 4.54(2H, ABq, J = 12.0 Hz), 4.59(3H, t, J = 6.6 Hz), 4.95(1H, d, J =
10 4.8 Hz), 5.17 and 5.26(2H, ABq, J = 11.7 Hz), 5.90(1H, dd, J = 4.8 and 8.7 Hz), 6.84(1H,
s), 6.90(2H, d, J = 9.0 Hz), 7.24-7.38(12H, m), 7.48(1H, d, J = 8.7 Hz), 8.50(1H, brs).

IR (KBr) cm^{-1} : 3283, 3062, 3031, 2978, 2836, 1789, 1721, 1613, 1549, 1515, 1454, 1386, 1369, 1302, 1246, 1158, 1096, 1063, 1031.

MS(ESI): 910⁺(M+H⁺).

15 Elemental analysis as $\text{C}_{42}\text{H}_{41}\text{Cl}_2\text{N}_5\text{O}_{10}\text{S}_2 \cdot 0.3 \text{ CHCl}_3 \cdot 0.7 \text{ H}_2\text{O}$.

Calc. : C, 52.96 ; H, 4.49 ; N, 7.30 ; S, 6.69 ; Cl, 10.72 (%).

Found : C, 52.91 ; H, 4.34 ; N, 7.33 ; S, 6.64 ; Cl, 10.74 (%).

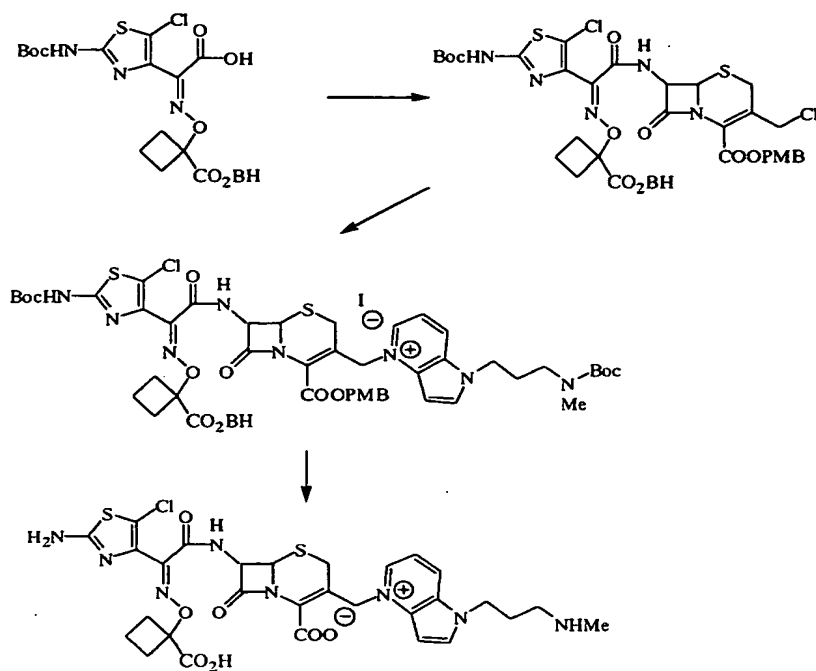
quaternary salt ester :

¹H-NMR (d_6 -DMSO) δ : 1.37(9H, s), 1.46(9H, s), 2.03(2H, m), 2.77(3H, brs), 2.87(2H, t,
20 J = 6.6 Hz), 3.18(2H, t, J = 6.6 Hz), 3.28 and 3.35(2H, m), 3.75(3H, s), 4.36(2H, t, J = 6.3
Hz), 4.43(2H, t, J = 6.6 Hz), 5.15(1H, d, J = 4.8 Hz), 5.21 and 5.29(2H, ABq, J = 11.7 Hz),
5.66 and 5.72(2H, ABq, J = 15.0 Hz), 5.94(1H, dd, J = 4.8 and 9.0 Hz), 6.75(1H, s),
6.88(2H, d, J = 8.7 Hz), 6.99(1H, d, J = 3.3 Hz), 7.20-7.40(12H, m), 7.78(1H, dd, J = 6.0
and 8.1 Hz), 8.43(1H, d, J = 3.3 Hz), 8.59(1H, d, J = 6.0 Hz), 8.88(1H, d, J = 8.1 Hz),
25 9.72(1H, d, J = 9.0 Hz), 12.1(1H, brs).

IR (KBr) cm^{-1} : 3424, 3061, 3031, 2975, 2934, 1791, 1719, 1685, 1630, 1613, 1548, 1515, 1495, 1455, 1392, 1367, 1247, 1156, 1029.

MS(ESI): 1163⁺($\text{C}_{53}\text{H}_{64}\text{ClN}_8\text{O}_{12}\text{S}_2$).

30 Example 23



¹H-NMR (D₂O) δ : 1.90(2H, m), 2.31(4H, m), 2.44(2H, m), 2.68(3H, s), 3.05(2H, t, J = 8.1 Hz), 3.17 and 3.39 (2H, ABq, J = 18.0 Hz), 4.54(2H, t, J = 6.9 Hz), 5.20(1H, d, J = 4.8 Hz), 5.56 and 5.69(2H, ABq, J = 15.0 Hz), 5.83(1H, d, J = 4.8 Hz), 7.04(1H, d, J = 3.3 Hz), 7.69(1H, dd, J = 6.3 and 8.4 Hz), 8.12(1H, d, J = 3.3 Hz), 8.60(1H, d, J = 8.4 Hz), 8.64(1H, d, J = 6.3 Hz).

IR (KBr) cm⁻¹: 3398, 2948, 1774, 1610, 1538, 1498, 1458, 1392, 1287, 1236, 1158, 1120, 1064, 1032.

MS(ESI): 703⁺(M+H⁺).

10 Elemental analysis as C₂₉H₃₁ClN₈O₇S₂ · 6.5 H₂O.

Calc. : C, 42.46 ; H, 5.41 ; N, 13.66 ; Cl, 4.32 ; S, 7.82 (%).

Found : C, 42.34 ; H, 4.87 ; N, 13.71 ; Cl, 4.39 ; S, 7.79 (%).

7-side chain

¹H-NMR (d₆-DMSO) δ : 1.47(9H, s), 1.75-2.00(2H, m), 2.20-2.38(2H, m), 2.44-2.54(2H, m), 6.82(1H, s), 7.1-7.5(10H, m), 12.0(1H, brs).

IR (KBr) cm⁻¹: 3209, 3064, 3031, 2980, 2955, 1719, 1619, 1554, 1495, 1454, 1394, 1370, 1295, 1249, 1204, 1155, 1067, 1037.

MS(ESI): 586⁺(M+H⁺).

Elemental analysis as C₂₈H₃₀ClN₈O₇S₁ · 1.3 H₂O.

20 Calc. : C, 55.18 ; H, 5.06 ; N, 6.89 ; Cl, 5.82 ; S, 5.26 (%).

Found : C,55.17 ; H,4.92 ; N,7.28 ; Cl,5.65 ; S,5.24 (%).

3-chloromethyl compound:

$^1\text{H-NMR}$ (CDCl_3) δ : 1.53(9H, s), 2.05-2.18(2H, m), 2.47-2.78(4H, m), 3.26

and 3.51(2H, ABq, $J = 18.3$ Hz), 3.82(3H, s), 4.40 and 4.56(2H, ABq, $J =$

5 12.0 Hz), 4.96(1H, d, $J = 4.8$ Hz), 5.24(1H, d, $J = 5.1$ Hz), 5.21 and 5.27(2H, ABq, $J =$
12.0 Hz), 5.97(1H, dd, $J = 5.1$ and 9.6 Hz), 6.90(2H, d, $J = 8.7$ Hz), 6.92(1H, s), 7.25-
7.31(10H, m), 7.35(2H, d, $J = 8.7$ Hz), 7.44(1H, d, $J = 9.6$ Hz) , 8.00(1H, s).

IR (KBr) cm^{-1} : 3378, 3285, 3063, 3031, 2978, 2836, 1790, 1722, 1613, 1585, 1549, 1515,
1454, 1385, 1368, 1300, 1247, 1203, 1156, 1112, 1098, 1063, 1034.

10 MS(ESI):936 $^+$ ($\text{M}+\text{H}^+$).

quarternary ammonium salt ester :

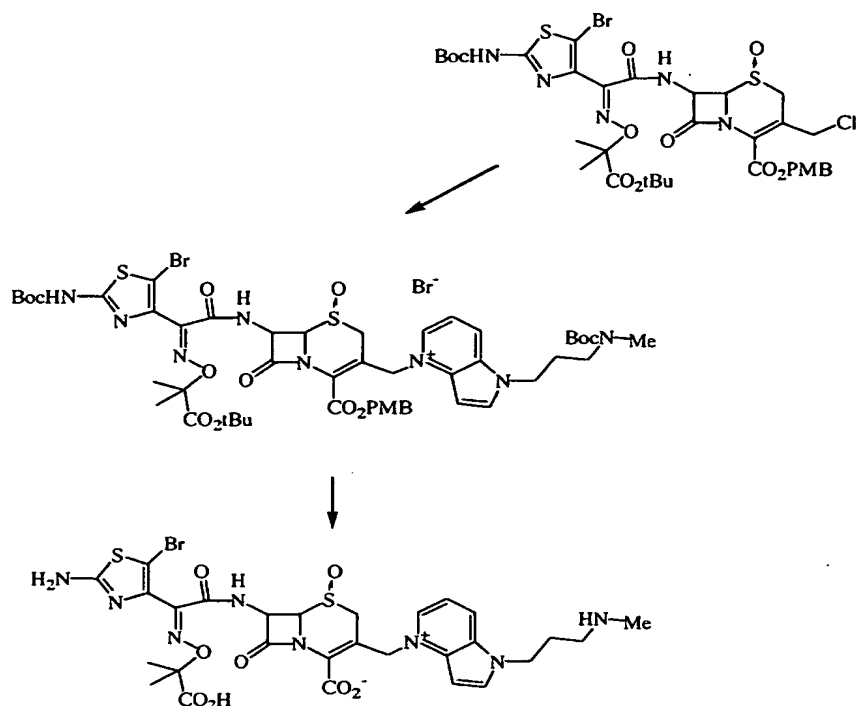
$^1\text{H-NMR}$ ($\text{d}_6\text{-DMSO}$) δ : 1.36(9H, brs), 1.46(9H, s), 1.79-2.09(2H, m), 2.03(2H, quintet-
like), 2.30-2.61(4H, m), 2.77(3H, brs), 3.17(2H, t-like), 3.30 and 3.42(2H, ABq, $J = 13.2$
Hz), 3.76(3H, s), 4.43(2H, t-like), 5.21(1H, d, $J = 4.8$ Hz), 5.22 and 5.31(2H, ABq, $J =$

15 11.7 Hz), 5.71(2H, brs), 6.01(1H, dd, $J = 4.8$ and 8.7 Hz), 6.82(1H, s), 6.90(2H, d, $J = 8.4$
Hz), 6.96(1H, d, $J = 3.3$ Hz), 7.21-7.44(12H, m), 7.78(1H, dd, $J = 6.3$ and 8.1 Hz),
8.42(1H, d, $J = 3.3$ Hz), 8.63(1H, d, $J = 6.3$ Hz), 8.88(1H, d, $J = 8.1$ Hz), 9.77(1H, d, $J =$
8.7 Hz), 12.1(1H, brs).

IR (KBr) cm^{-1} :3424, 3061, 2975, 1791, 1718, 1685, 1630, 1613, 1584, 1550, 1515, 1495,

20 1455, 1392, 1367, 1298, 1248, 1155, 1123, 1065, 1030, 1018.

Example 24



¹H-NMR (D₂O) δ : 1.50 (6H, br s), 2.30(2H, q like), 2.69(3H, s), 3.06(2H, t, J = 7.8 Hz), 3.38 and 3.63(2H, ABq, J = 18.3 Hz), 4.52(2H, m), 4.98(1H, d, J = 4.8 Hz), 5.63 and 5.75(2H, ABq, J = 15.3 Hz), 6.05(1H, d, J = 4.8 Hz), 7.06(1H, d, J = 3.3 Hz), 7.69(1H, dd, J = 6.0, 8.1 Hz), 8.13(1H, d, J = 3.3 Hz), 8.59(1H, d, J = 8.1 Hz), 8.67(1H, d, J = 6.0 Hz).

IR (KBr) cm⁻¹: 3412, 1784, 1618, 1535, 1396, 1361, 1159, 858, 760 .

Elemental analysis as C₂₈H₃₁N₈O₈S₂Br · 6.4H₂O

Calc. : C, 38.79; H, 5.09; N, 12.93; S, 7.40; Br, 9.22 (%).

Found : C, 38.82; H, 4.85; N, 12.90; S, 7.43; Br, 9.02 (%).

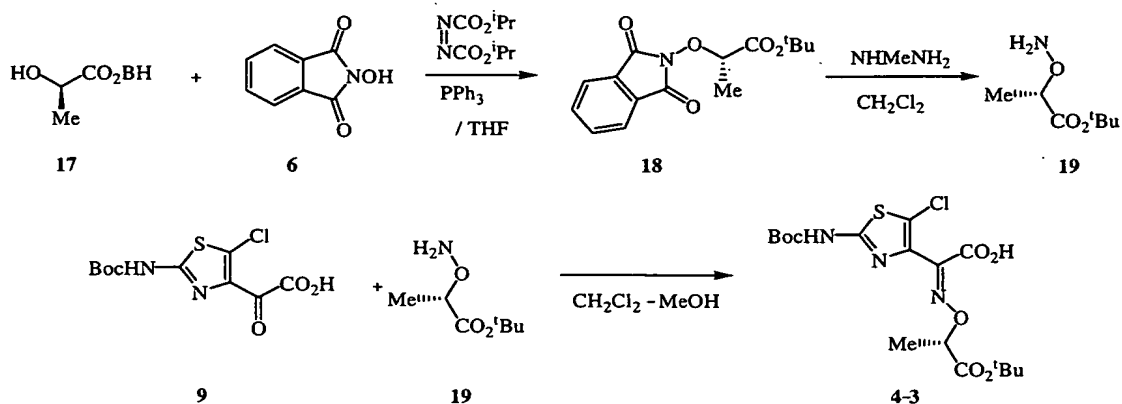
10 quarternary ammonium salt ester (S-Oxide) :

IR (KBr) cm⁻¹: 3427, 2978, 2935, 1802, 1722, 1687, 1549, 1516, 1458, 1390, 1367, 1250, 1153, 1030, 766 .

3-chloromethyl compound (S-Oxide) :

¹H-NMR (CDCl₃) δ : 1.42(9H, s), 1.52(9H, s), 1.61(6H, br s), 3.43 and 3.82(2H, ABq, J = 18.6 Hz), 3.82(3H, s), 4.24 and 5.03(2H, ABq, J = 12.6 Hz), 4.59(1H, dd, J = 1.2, 5.1 Hz), 5.24 and 5.30(2H, ABq, J = 12 Hz), 6.19(1H, dd, J = 5.1, 9.6 Hz), 6.92 and 7.37(4H, A2B2q, J = 6.6 Hz), 7.94(1H, d, J = 10.2 Hz), 8.37(1H, br s).

Example 25



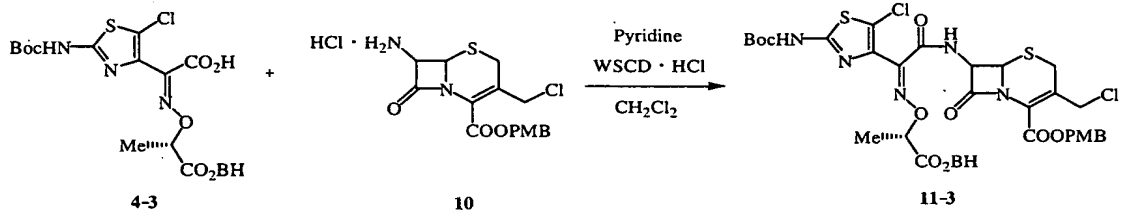
(1) To a solution of compound 17 (4.85g) in THF 38ml, were added triphenylphosphine (5.71g) and hydroxyphthalimide (3.55g) and the mixture was stirred under ice-cooling. Diisopropyl azodicarbonate (4.3 ml) was added dropwise and the mixture was allowed to stand at 4°C overnight. The mixture was concentrated in vacuum, purified with silica gel chromatography, and crystallized from ether / hexane to give compound 18 (7.6g).

¹H-NMR (CDCl₃) δ: 1.67(3H, d, J = 7.2 Hz), 5.05(1H, q, J = 7.2 Hz), 6.93

(1H, s), 7.22-7.32(10H, m), 7.70-7.79(4H, m).

IR (KBr) cm⁻¹: 1791, 1736, 1284, 700.

FABMS: m/z 402 [M+H]⁺, 803 [2M+H]⁺.



(2) To a solution of compound 18 (4.82g) in CH₂Cl₂ 12 ml, was added at -25°C methylhydrazine 0.63ml and the mixture was stirred for 1.5 hr. The obtained crystal was collected by filtration and the filtrate was diluted with MeOH 25ml. Carboxylic acid 9 (3.7g) was added under ice-cooling and the mixture was stirred for 2 hr and allowed to stand at 4°C overnight. The reaction solution was concentrated in vacuum and dissolved to AcOEt, which was washed with NaHCO₃ water, hydrochloric acid water, and saline, then dried over MgSO₄ and evaporated to give compound 4-3 (4.74g).

¹H-NMR (d₆-DMSO) δ: 1.46(3H, d, J = 6.9 Hz), 1.47(9H, s), 5.00(1H, q, J = 6.9

Hz), 6.85(1H, s), 7.26-7.42(10H, m), 12.06(1H, s).

IR (KBr) cm⁻¹: 3422, 3193, 3062, 3032, 2983, 1740, 1719, 1602, 1554, 1453,

1370, 1250, 1155, 1096, 1038, 967, 744, 699.

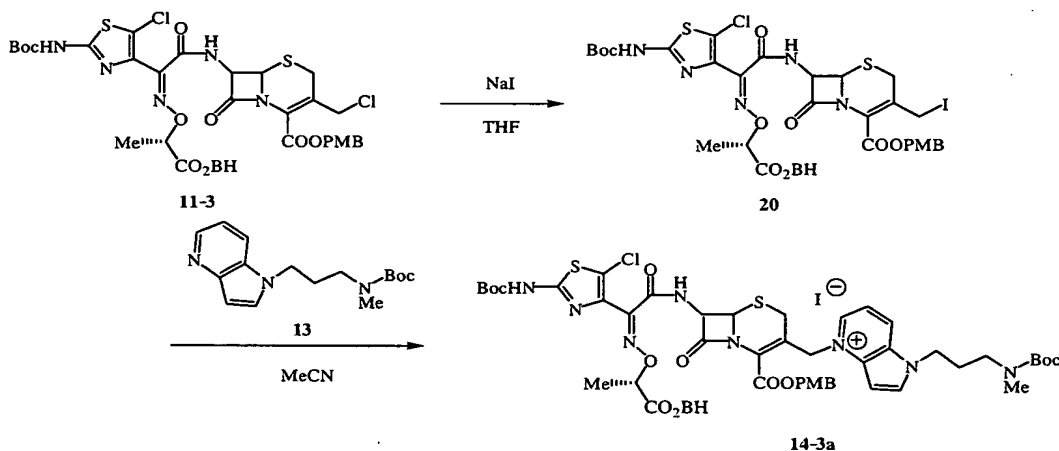
FABMS: m/z 560 $[M+H]^+$, 1119 $[2M+H]^+$.

(3) To a solution of carboxylic acid 4-3 (3.50g, 6.25mmol) and ACLE \cdot HCl 10 (2.53g 6.25mmol) in CH_2Cl_2 21ml, were added WSCD \cdot HCl (1.20g 1eq) and Pyridine (0.51ml, 1.0eq) under ice-cooling, and the mixture was stirred at the same temperature for 1 hr. The reaction solution was washed with brine, dried with anhydrous $MgSO_4$, concentrated in vacuum, and purified with silica gel chromatography to give a foam-like residue 11-3 (4.60g).

1H -NMR ($CDCl_3$) δ : 1.53(9H, s), 1.64(3H, d, $J = 7.2$ Hz), 3.39 and 3.58(2H, ABq, $J = 18.3$ Hz), 3.81(3H, s), 4.42 and 4.59(2H, ABq, $J = 12$ Hz), 4.97(1H, d, $J = 5.1$ Hz), 5.08(1H, q, $J = 7.2$ Hz), 5.20 and 5.27(2H, ABq, $J = 11.7$ Hz), 6.01(1H, dd, $J = 5.1, 9.3$ Hz), 6.88-6.91(3H, m), 7.06-7.35(12H, m), 7.85(1H, d, $J = 9.3$ Hz), 8.15(1H, br s).

IR (KBr) cm^{-1} : 3281, 2980, 2935, 2836, 1790, 1719, 1612, 1552, 1515, 1454, 1369, 1247, 1155, 1035, 700.

FABMS: m/z 910 $[M+H]^+$.



(4) To a solution of Cl-compound 11-3 (4.60g, 5.05mmol) in THF cooled to $13^\circ C$, was added NaI (2.65g 3.5eq) and the mixture was stirred for 30 min. The reaction solution was poured to $Na_2S_2O_3$ aq. - EtOAc and the organic layer was separated, washed with brine, dried with anhydrous $MgSO_4$, concentrated in vacuum to give a foam-like residue 20 (5.07g).

1H -NMR ($CDCl_3$) δ : 1.53(9H, s), 1.65(3H, d, $J = 7.2$ Hz), 3.39 and 3.67(2H, ABq, $J = 17.7$ Hz), 3.81(3H, s), 4.33 and 4.45(2H, ABq, $J = 9.3$ Hz), 4.96(1H, d, $J = 5.1$ Hz), 5.08(1H, q, $J = 7.2$ Hz), 5.20 and 5.28(2H, ABq, $J = 11.7$ Hz), 5.95(1H, dd, $J = 5.1, 9.0$ Hz), 6.88-6.92(3H, m), 7.23-7.39(12H, m), 7.78(1H, d, $J = 9.0$ Hz), 8.01(1H, br s).

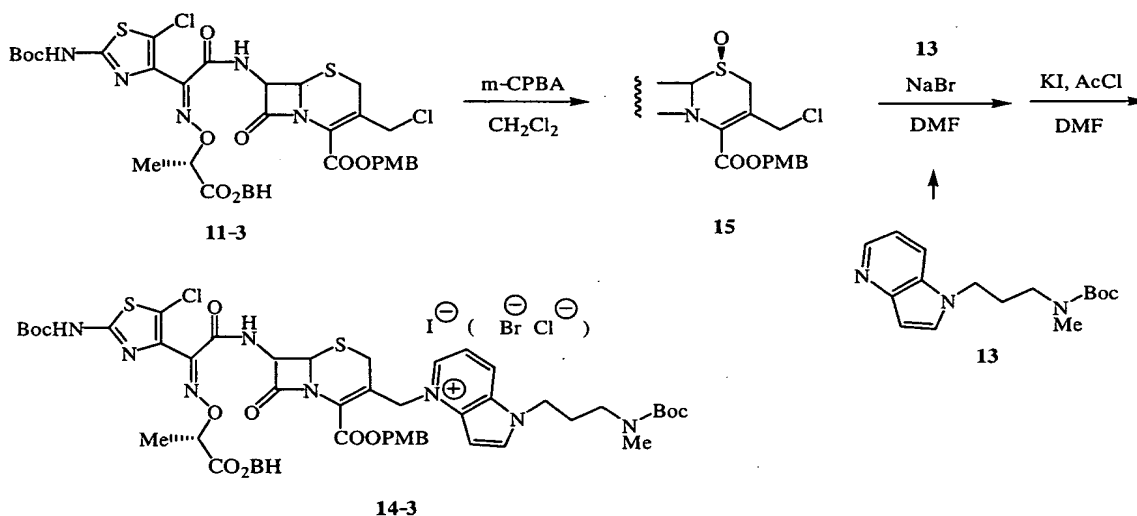
IR (KBr) cm^{-1} : 3383, 3284, 2980, 2836, 1790, 1719, 1613, 1551, 1516, 1369, 1246, 1153, 1037, 700.

ABMS: m/z 1002 $[M+H]^+$.

(5) To a solution of a material for 3-side chain, 13 (174mg, 0.60mmol) in MeCN 1ml, was added iode compound 20 (570mg, 0.60mmol) under ice-cooling, and the mixture was stirred at the same temperature for 3 hr and at room temperature for 2 hr. A mixture of Toluene/ Et₂O/n-Hexane (1:30:30) was added dropwise thereto and the precipitated powder was collected by filtration to give quaternary salt 14-3a (675mg).

¹H-NMR (CDCl₃) δ : 1.46(9H, s), 1.51(9H, s), 1.61(3H, d, J = 7.2 Hz), 2.21(2H, m), 2.88(3H, s), 3.19 and 3.89(2H, ABq, J = 18.9 Hz), 3.33(2H, m), 3.80(3H, s), 4.42(2H, t like), 5.04-5.15(4H, m), 5.22 and 5.30(2H, ABq, J = 12 Hz), 5.84 and 5.75(2H, ABq, J = 14.7 Hz), 5.98(1H, dd, J = 5.1, 8.7 Hz), 6.89(3H, m), 7.25-7.36(12H, m), 7.54(1H, t like), 7.75(1H, d, J = 7.8 Hz), 8.25(1H, m), 8.56(1H, d, J = 8.7 Hz), 8.95(1H, d, J = 5.7 Hz).

IR (KBr) cm⁻¹: 3423, 2976, 2932, 1792, 1718, 1687, 1613, 1550, 1515, 1496, 1454, 1367, 1248 1154, 759, 701.



(6) To a solution of Cl-compound 11-3 (2.13g, 2.33mmol) in CH₂Cl₂ 10ml, was added dropwise a solution of m-CPBA (purity: >65%, 495mg 0.81eq) in CH₂Cl₂ 8ml at -50 °C and the mixture was stirred at the same temperature for 30 min. 5% Na₂S₂O₃ aq. was added thereto and the organic layer was washed with NaHCO₃ aq. and brine, dried over anhydrous MgSO₄, then concentrated in vacuum. To the obtained foam-like residue was added Et₂O/n-Hexane to give oxide 15 (about 2g) as powder.

¹H-NMR (CDCl₃) δ : 1.53(9H, s), 1.64(3H, d, J = 7.2 Hz), 3.29 and 3.70(2H, ABq, J = 18.6 Hz), 3.81(3H, s), 4.23 and 4.99(2H, ABq, J = 12.6 Hz), 4.44(1H, d, J = 5.1 Hz), 5.10(1H, q, J = 7.2 Hz), 5.26 (2H, m), 6.16(1H, dd, J = 5.1, 9.6 Hz), 6.88-6.94(3H, m), 7.25-7.375(12H, m), 7.90(1H, d, J = 9.6 Hz), 8.32(1H, br s).

IR (KBr) cm⁻¹: 3425, 2979, 2937, 1804, 1720, 1613, 1553, 1516, 1454, 1369,

1249 1155, 1037, 701 .

(7-1) To a solution of a material for 3-side chain, 13 (324mg 1.1eq), in DMF 1.8ml, were added oxide 15 (1.22g, 1.31mmol) and NaBr (271mg 2eq) and the mixture was stirred in nitrogen atmosphere at room temperature for 1.5 hr. DMF 2ml and KI 1.28g were added thereto and the mixture was cooled to -40°C, to which was added dropwise AcCl 0.40ml and the mixture was stirred at -10°C for 3 hr. The reaction solution was poured to a phosphate buffer of pH 6 containing NaCl and Na₂S₂O₃, then the precipitates were collected by filtration, dissolved to acetone, and concentrated in vacuum. To the residue was added Et₂O/n-Hexane to give quaternary salt 14-3 (1.77g).

¹H-NMR (CDCl₃) δ : 1.48(9H, s), 1.51(9H, s), 1.62(3H, d, J = 7.2 Hz), 2.21(2H, m), 2.91(3H, s), 3.24 and 3.82(2H, ABq, J = 18.9 Hz), 3.36(2H, m), 3.81(3H, s), 4.43(2H, t like), 5.09(1H, q, J = 7.2 Hz), 5.16(1H, d, J = 5.1 Hz), 5.24 and 5.31(2H, ABq, J = 11.7 Hz), 5.58 and 5.75(2H, ABq, J = 14.7 Hz), 5.99(1H, dd, J = 5.1, 8.7 Hz), 6.86(1H, s), 6.87(2H, d, J = 8.7 Hz), 7.00(1H, br s), 7.24 - 7.38(12H, m), 7.55(1H, t like), 7.78(H, d, J = 8.7 Hz), 8.25(1H, br s), 8.47(1H, d, J = 10.2 Hz), 8.50(1H, d, J = 6 Hz).

IR (KBr) cm⁻¹: 3423, 2976, 2932, 1792, 1718, 1687, 1613, 1248 1154, 759, 701 .

(7-2) To a solution of a material for 3-side chain, 13 (174mg, 0.60mmol) in MeCN 1ml, was added iode compound 20 (570mg, 0.60mmol as reduced purity) under ice-cooling and the mixture was stirred at the same temperature for 3 hr and at room temperature for 2 hr. A mixture of Toluene/Et₂O/n-Hexane (1:30:30) was added dropwise thereto and the precipitated powder was collected by filtration to give quaternary salt 14-3a 675mg.

(8) To a solution of quaternary salt 14-3 (about 1.3 mmol) in CH₂Cl₂ - MeNO₂ 30ml and anisole 1.7 ml, was added an AlCl₃-MeNO₂ solution (1.5M, 7 ml) in nitrogen atmosphere under ice-cooling and the mixture was stirred for 1 hr. Ice, 1N HCl-CH₃CN and Et₂O were added thereto and the water layer was separated, concentrated in vacuum, and subjected to HP-20 chromat. The collected eluate was lyophilized to give compound 16-3 (450 mg) as powder.

¹H-NMR (D₂O) δ : 1.43 (3H, d, J = 7.2 Hz), 2.31(2H, q like), 2.68(3H, s), 3.05(2H, t, J = 8 Hz), 3.18 and 3.37(2H, ABq, J = 18 Hz), 4.53(2H, t like), 4.65 (1H, q, J = 7.2 Hz), 5.17(1H, d, J = 4.8 Hz), 5.54 and 5.70(2H, ABq, J = 15 Hz), 5.86(1H, d, J = 4.5 Hz), 7.03(1H, d, J = 3.6 Hz), 7.69(1H, dd, J = 6, 8.4 Hz), 8.13(1H, d, J = 3.6 Hz), 8.60(1H, d, J = 8.4 Hz), 8.64(1H, d, J = 6 Hz).

IR (KBr) cm⁻¹: 3398, 1775, 1603, 1541, 1392, 1363, 1320, 1286, 1033, 762.

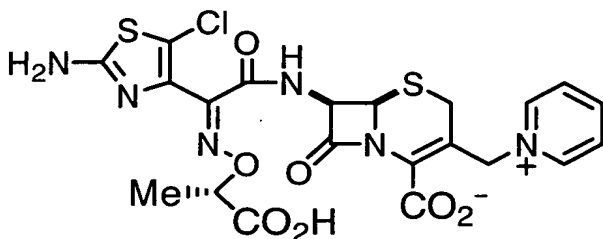
Positive ESIMS: m/z 677 [M+H]⁺ . Negative ESIMS: m/z 675 [M-H]⁻ .

Elemental analysis as $C_{27}H_{29}N_8O_7S_2Cl \cdot 6.2H_2O$

Calc. : C,41.11; H,5.29; N,14.20; S,8.13; Cl,4.49 (%).

Found : C,40.88; H,4.88; N,14.23; S,8.05; Cl,4.57 (%).

5 Example 26



1H -NMR (D_2O) δ : 1.51 (3H, d, J = 7.25 Hz), 3.22 and 3.64 (Abq, J = 17.9 Hz), 4.83 (1H, q, J = 7.2Hz), 5.28 (1H, d, J = 4.8 Hz), 5.35 and 5.58 (2H, ABq, J = 14.6 Hz), 5.90 (1H, d, J = 4.8Hz), 8.09 (2H, t-like), 8.57 (2H, t, J = 7.8 Hz), 8.95 (2H, d, J = 5.7 Hz).

10 IR (KBr) cm^{-1} : 3410, 3060, 1780, 1674, 1627, 1538, 1481, 1445, 1389, 1341, 1219, 1186, 1153, 1100, 1035.

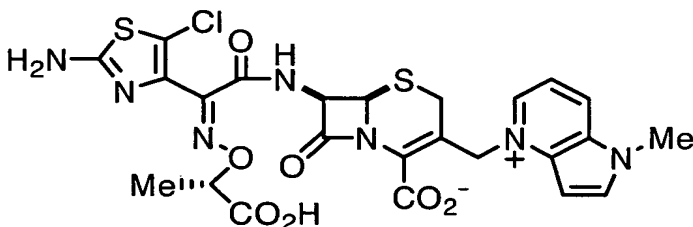
MS(ESI): 567⁺ (M+H)⁺.

Elementary Analysis as $C_{21}H_{19}ClN_6O_7S_2 \cdot 2.9 H_2O$.

Calculated : C,40.73 ; H,4.04 ; N,13.57 ; Cl,5.73; S,10.36 (%).

15 Found : C,40.67 ; H,3.87 ; N,13.45 ; Cl,5.50; S,10.36 (%).

Example 27



1H -NMR (d_6 -DMSO) δ : 1.36 (3H, d, J = 7.1 Hz), 2.97 and 3.25 (2H, Abq, J = 17.3 Hz), 4.03 (3H, s), 4.55 (1H, q, J = 7.1 Hz), 4.97 (1H, d, J = 5.1 Hz), 5.61-5.72 (3H, m), 5.60 and 5.73 (2H, ABq, J = 15.2 Hz), 7.37 (1H, d, J = 3.3 Hz), 7.41 (1H, s), 7.78 (1H, dd, J = 6.3, 8.2 Hz), 8.28 (1H, d, J = 3.3 Hz), 8.74 (1H, d, J = 8.2), 9.16 (1H, d, J = 6.3 Hz), 9.61 (1H, brs).

20 IR (KBr) cm^{-1} : 3423, 2986, 1778, 1674, 1618, 1538, 1500, 1469, 1416, 1368, 1324, 1281, 1222, 1187, 1154, 1094, 1062, 1032. ..

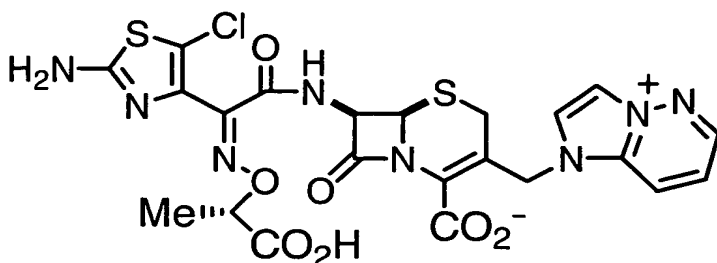
MS(ESI): 620⁺ (M+H)⁺.

Elementary Analysis as $C_{24}H_{22}ClN_7O_7S_2 \cdot 2.6 H_2O$.

Calculated : C,43.22 ; H,4.11 ; N,14.70 ; Cl,5.32; S,9.62 (%).

Found : C,43.16 ; H,3.99 ; N,14.88 ; Cl,5.12; S,9.61 (%).

Example 28



5

¹H-NMR (D₂O) δ : 1.50 (3H, d, J = 6.9 Hz), 3.20 and 3.58 (2H, ABq, J = 17.7 Hz), 4.80 and 4.84 (2H, ABq, J = 6.9 Hz), 5.24 (1H, d, J = 4.8 Hz), 5.37 and 5.42 (2H, ABq, J = 16.2 Hz), 5.87 (1H, d, J = 4.8 Hz), 7.90 (1H, dd, J = 4.5, 9.4 Hz), 8.25 (1H, d, J = 2.3 Hz), 8.44 (1H, d, J = 2.3 Hz), 8.66 (1H, d, J = 9.4 Hz), 8.94 (1H, dd, J = 1.5, 4.5 Hz).

10 IR (KBr) cm⁻¹: 3416, 3136, 2939, 1776, 1674, 1625, 1535, 1447, 1383, 1346, 1317, 1232, 1185, 1155, 1100, 1066, 1035.

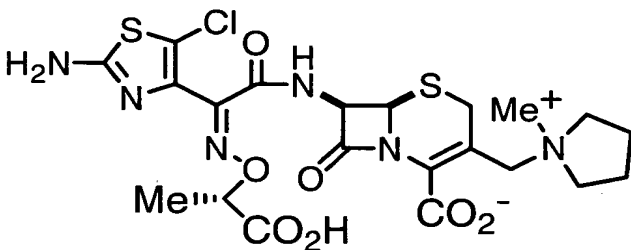
MS(FAB): 607⁺ (M+H)⁺.

Elementary Analysis as C₂₂H₁₉ClN₈O₇S₂ · 2.8 H₂O.

Calculated : C,40.19 ; H,3.77 ; N,17.04 ; Cl,5.39; S,9.75 (%).

15 Found : C,40.10 ; H,3.56 ; N,17.01 ; Cl,5.20; S,9.73 (%).

Example 29



20 ¹H-NMR (D₂O) δ : 1.55 (3H, d, J = 7.2 Hz), 2.22 (4H, brs), 2.99 (3H, s), 3.46 and 3.92 (2H, ABq, J = 17.0 Hz), 3.53 (4H, m), 3.99 and 4.74 (2H, ABq, J = 13.79 Hz), 4.85 (1H, q, J = 7.2 Hz), 5.36 (1H, d, J = 5.1 Hz), 5.90 (1H, d, J = 5.1 Hz).

IR (KBr) cm⁻¹: 3416, 1780, 1676, 1616, 1538, 1459, 1345, 1285, 1236, 1180, 1097, 1068, 1036.

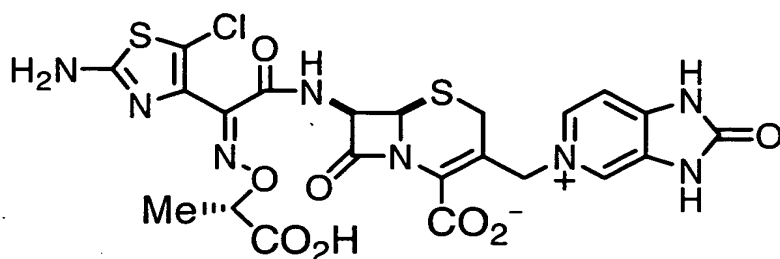
MS(FAB): 573⁺ (M+H)⁺.

Elementary Analysis as C₂₁H₂₅ClN₆O₇S₂ · 4.0 H₂O.

25 Calculated : C,39.10 ; H,5.16 ; N,13.03 ; Cl,5.50; S,9.94 (%).

Found : C,38.86 ; H,4.64 ; N,13.00; Cl,5.30; S,9.90 (%).

Example 30



¹H-NMR (d₆-DMSO) δ : 1.37 (3H, d, J = 7.1 Hz), 3.15 and 3.50 (ABq, J = 17.6 Hz), 4.54 (1H, q, J = 7.1 Hz), 4.96 and 5.58 (2H, ABq, J = 13.4 Hz), 5.11 (1H, d, J = 4.9 Hz), 5.73 (1H, dd, J = 4.9, 8.9 Hz), 7.41 (2H,s), 7.52 (1H, d, J = 6.6 Hz), 8.70 (2H, d, J = 6.6 Hz), 9.14 (1H, s), 9.75 (1H, brs).

IR (KBr) cm⁻¹: 3414, 3086, 1738, 1661, 1620, 1527, 1446, 1390, 1351, 1307, 1210, 1118, 1066, 1036.

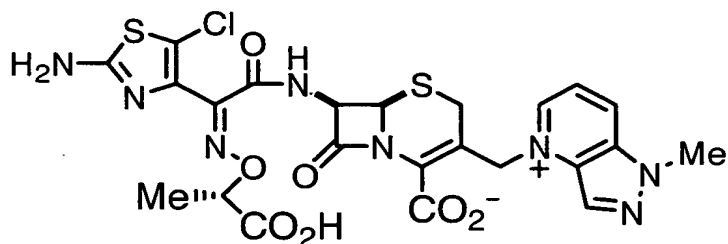
MS(ESI): 623⁺ (M+H)⁺.

10 Elementary Analysis as C₂₂H₁₉ClN₈O₈S₂ · 3.7 H₂O.

Calculated : C,38.31 ; H,3.86 ; N,16.25 ; Cl,5.14; S,9.30 (%).

Found : C,38.18 ; H,3.51 ; N,16.22 ; Cl,4.85; S,9.24 (%).

Example 31



¹H-NMR (d₆-DMSO) δ : 1.36 (3H, d, J = 7.1 Hz), 3.03 and 3.32 (ABq, J = 17.6 Hz), 4.29 (3H, s), 4.55 (1H, q, J = 7.1 Hz), 5.00 (1H, d, J = 5.0 Hz), 5.69 (1H, dd, J = 5.0, 8.6 Hz), 5.75 and 5.818 (2H, ABq, J = 14.1 Hz), 7.42 (2H,s), 8.12 (1H, dd, J = 5.6, 8.8 Hz), 9.08 (1H, d, J = 8.8 Hz), 9.15 (1H, s), 9.46 (1H, d, J = 5.6 Hz), 9.56 (1H, d, J = 8.6 Hz).

20 IR (KBr) cm⁻¹: 3415, 1779, 1675, 1617, 1538, 1483, 1442, 1392, 1372, 1348, 1291, 1236, 1188, 1155, 1100, 1063, 1034.

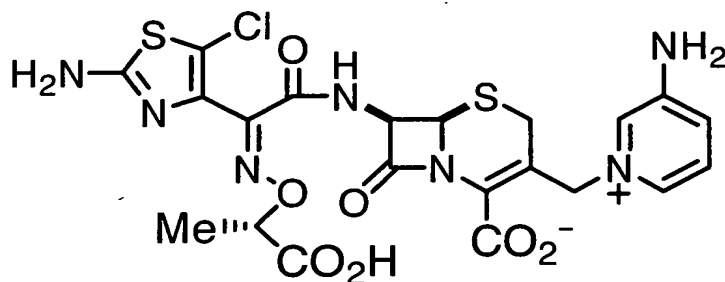
MS(ESI): 621⁺ (M+H)⁺.

Elementary Analysis as C₂₃H₂₁ClN₈O₇S₂ · 3.1 H₂O.

Calculated : C,40.81; H,4.05; N,16.55; Cl,5.24; S,9.47 (%).

25 Found : C,40.85; H,3.85; N,16.73; Cl,5.01; S,9.46 (%).

Example 32



¹H-NMR (d₆-DMSO) δ : 1.39 (3H, d, J = 7.1 Hz), 3.01 and 3.46 (2H, ABq, J = 17.6 Hz), 4.56 (1H, q, J = 7.1 Hz), 5.00 and 5.55 (2H, ABq, J = 13.4 Hz), 5.06 (1H, d, J = 5.1 Hz), 5.70 (1H, dd, J = 5.1 Hz), 6.74 (2H, brs), 7.42 (2H, brs), 7.55 (1H, d, J = 8.5 Hz), 7.68 (1H, dd, J = 8.5, 5.7 Hz), 8.38 (1H, d, J = 5.7 Hz), 8.51 (1H, brs), 9.67 (1H, brs).

IR (KBr) cm⁻¹: 3351, 3208, 1777, 1629, 1538, 1512, 1445, 1391, 1346, 1232, 1190, 1155, 1098, 1065, 1034.

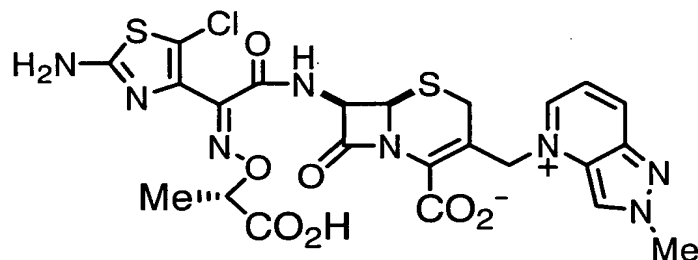
MS(ESI): 582⁺ (M+H)⁺.

10 Elementary Analysis as C₂₁H₂₀ClN₇O₇S₂ · 3.6 H₂O.

Calculated : C,38.99; H,4.24; N,15.16; Cl,5.48; S,9.91 (%).

Found : C,38.84; H,3.84; N,15.23; Cl,5.34; S,9.67 (%).

Example 33



¹H-NMR (d₆-DMSO) δ : 1.37 (3H, d, J = 6.9 Hz), 3.10 and 3.34 (2H, ABq, J = 17.3 Hz), 4.39 (3H, s), 4.55 (1H, q, J = 6.9 Hz), 5.01 (1H, d, J = 4.9 Hz), 5.60 and 5.73 (2H, ABq, J = 14.3 Hz), 5.68 (1H, dd, J = 4.9, 9.0 Hz), 7.42 (2H, s), 7.97 (1H, dd, J = 5.5, 8.6 Hz), 9.04 (1H, d, J = 8.6 Hz), 9.42 (1H, d, J = 5.5 Hz), 9.59 (2H, brs).

20 IR (KBr) cm⁻¹: 3419, 1778, 1634, 1615, 1538, 1454, 1408, 1356, 1329, 1295, 1235, 1176, 1156, 1100, 1073, 1035, 1011.

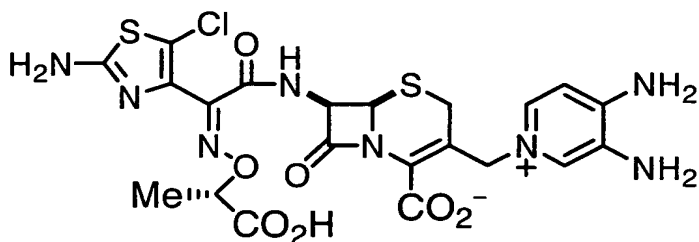
MS(ESI): 621⁺ (M+H)⁺.

Elementary Analysis as C₂₃H₂₁ClN₈O₇S₂ · 3.2 H₂O.

Calculated : C,40.70; H,4.07; N,16.51; Cl,5.22; S,9.45 (%).

25 Found : C,40.48; H,3.61; N,16.42; Cl,5.16; S,9.46 (%).

Example 34



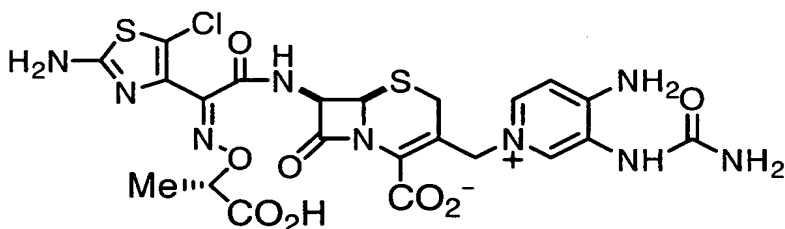
¹H-NMR (d₆-DMSO) δ : 1.39 (3H, d, J = 7.1 Hz), 2.95 and 3.41 (2H, ABq, J = 17.7 Hz), 4.57 (1H, q, J = 7.1 Hz), 4.70 and 5.22 (2H, ABq, J = 13.8 Hz), 5.05 (1H, d, J = 4.89 Hz), 5.66 (2H, brs), 5.71 (1H, dd, J = 4.8, 8.7 Hz), 6.73 (1H, d, J = 6.9 Hz), 7.42 (4H, brs), 7.98 (2H, m).

IR (KBr) cm⁻¹: 3379, 3213, 1775, 1645, 1577, 1542, 1446, 1360, 1308, 1235, 1184, 1156, 1065, 1035.

MS(ESI): 597⁺ (M+H)⁺.

- 10 Elementary Analysis as C₂₁H₂₁ClN₈O₇S₂ · 3.1 H₂O.
Calculated : C,38.63; H,4.20; N,17.16; Cl,5.43; S,9.82 (%).
Found : C,38.51; H,3.83; N,17.22; Cl,5.41; S,9.75 (%).

Example 35



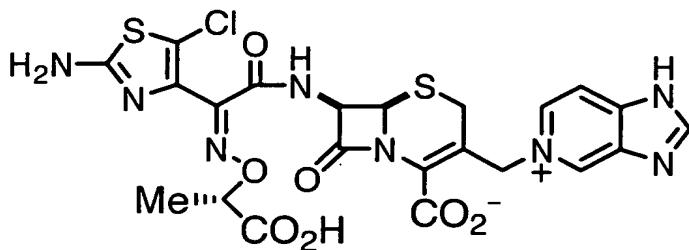
¹H-NMR (d₆-DMSO) δ : 1.40 (3H, d, J = 7.1 Hz), 3.09 and 3.48 (2H, ABq, J = 17.7 Hz), 4.57 (1H, q, J = 7.1 Hz), 4.85 and 5.22 (2H, ABq, J = 13.8 Hz), 5.09 (1H, d, J = 4.9 Hz), 5.76 (1H, dd, J = 4.9 Hz), 6.58 (2H, brs), 6.95 (1H, d, J = 6.5 Hz), 7.40 (2H, s), 7.96 (2H, brs), 8.28 (1H, d, J = 6.5 Hz), 8.82 (1H, brs), 9.25 (1H, brs), 9.77 (1H, brs).

- 20 IR (KBr) cm⁻¹: 3364, 3205, 1775, 1657, 1540, 1493, 1447, 1355, 1270, 1182, 1146, 1109, 1066, 1034.

MS(ESI): 640⁺ (M+H)⁺.

- Elementary Analysis as C₂₂H₂₂ClN₉O₈S₂ · 3.0 H₂O.
Calculated : C,38.07; H,4.07; N,18.16; Cl,5.11; S,9.24 (%).
25 Found : C,37.72; H,3.67; N,17.97; Cl,5.03; S,9.02 (%).

Example 36



¹H-NMR (d₆-DMSO) δ : 1.36 (3H, d, J = 7.0 Hz), 3.10 and 3.54 (2H, ABq, J = 17.6 Hz), 4.55 (1H, q, J = 7.0 Hz), 5.14 (1H, d, J = 5.0 Hz), 5.20 and 5.68 (2H, ABq, J = 13.8 Hz), 5.77 (1H, dd, J = 5.0, 9.1 Hz), 7.40 (2H, brs), 8.18 (1H, d, J = 6.6 Hz), 8.83 (1H, brs), 8.87 (1H, d, J = 6.6 Hz), 9.68 (1H, d, J = 9.1 Hz), 9.80 (1H, brs).

IR (KBr) cm⁻¹: 3412, 1777, 1614, 1539, 1444, 1377, 1305, 1187, 1108, 1066, 1036.

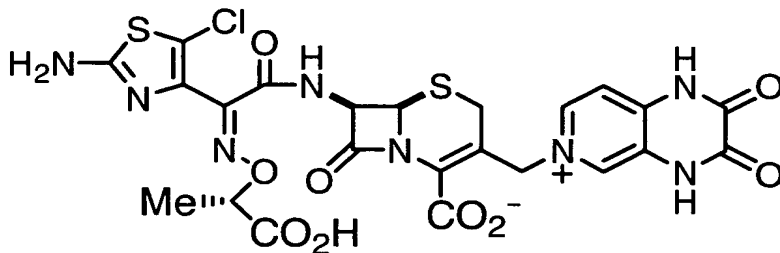
MS(ESI): 607⁺ (M+H)⁺ .

Elementary Analysis as C₂₂H₁₉ClN₈O₇S₂ · 2.7H₂O.

Calculated : C,40.30; H,3.75; N,17.09; Cl,5.41; S,9.78 (%).

Found : C,40.22; H,3.55; N,17.05; Cl,5.35; S,9.57 (%).

Example 37



¹H-NMR (d₆-DMSO) δ : 1.38 (3H, d, J = 7.1 Hz), 3.07 and 3.49 (2H, ABq, J = 17.4 Hz), 4.57 (1H, q, J = 7.1 Hz), 5.09 (1H, d, J = 4.8 Hz), 5.12 and 5.55 (2H, ABq, J = 13.5 Hz), 5.75 (1H, dd, J = 4.8, 8.2 Hz), 7.41 (2H, s), 7.48 (1H, d, J = 6.2 Hz), 8.70 (1H, d, J = 6.2 Hz), 8.90 (1H, brs), 9.62 (1H, d, J = 8.2 Hz).

IR (KBr) cm⁻¹: 3421, 3195, 3088, 2988, 1776, 1720, 1639, 1532, 1375, 1237, 1175, 1137, 1066, 1035..

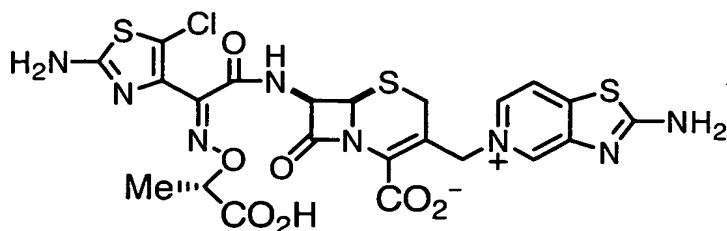
MS(ESI): 651⁺ (M+H)⁺ .

Elementary Analysis as C₂₃H₁₉ClN₈O₉S₂ · 3.1H₂O.

Calculated : C,39.08; H,3.59; N,15.85; Cl,5.02; S,9.07 (%).

Found : C,39.05; H,3.44; N,15.81; Cl,4.84; S,8.83 (%).

Example 38



¹H-NMR (d₆-DMSO) δ : 1.37 (3H, d, J = 6.9 Hz), 3.06 and 3.49 (2H, ABq, J = 17.6 Hz), 4.51 (1H, q, J = 6.9 Hz), 5.06 (1H, d, J = 4.7 Hz), 5.04 and 5.61 (2H, ABq, J = 12.9 Hz), 5.71 (1H, dd, J = 4.7, 8.9 Hz), 7.42 (2H, s), 8.40 (1H, d, J = 6.2 Hz), 8.64 (2H, s), 8.91 (1H, d, J = 6.2 Hz), 9.39 (1H, s), 9.60 (1H, brs).

IR (KBr) cm⁻¹: 3399, 3191, 1775, 1638, 1537, 1478, 1391, 1317, 1273, 1236, 1187, 1089, 1035.

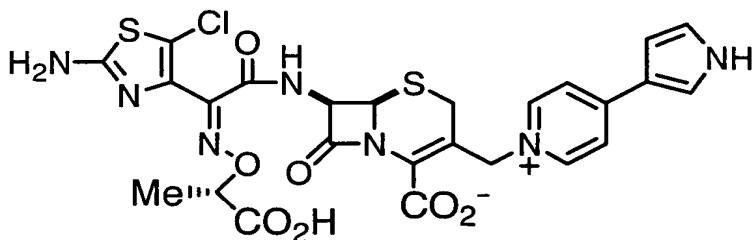
MS(ESI): 639⁺ (M+H)⁺.

Elementary Analysis as C₂₂H₁₉ClN₈O₇S₃ · 3.4H₂O

Calculated : C,37.73; H,3.71; N,16.00; Cl,5.06; S,13.74 (%).

Found : C,37.61; H,3.35; N,16.12; Cl,4.92; S,13.56 (%).

Example 39



¹H-NMR (d₆-DMSO) δ : 1.37 (3H, d, J = 6.9 Hz), 3.06 and 3.50 (2H, ABq, J = 17.7 Hz), 4.53 (1H, q, J = 6.9 Hz), 5.06 (1H, d, J = 4.7 Hz), 4.91 and 5.45 (2H, ABq, J = 12.5 Hz), 5.70 (1H, dd, J = 4.7, 8.79 Hz), 6.85 (1H, s), 7.01 (1H, s), 7.41 (2H, s), 7.96 (1H, s), 8.15 (2H, d, J = 5.7 Hz), 9.08 (2H, d, J = 5.7 Hz), 9.73 (1H, brs), 11.85 (1H, brs).

IR (KBr) cm⁻¹: 3410, 1774, 1636, 1560, 1474, 1354, 1218, 1152, 1107, 1037.

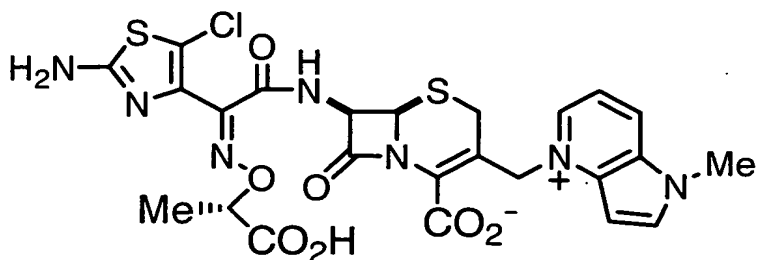
MS(ESI): 632⁺ (M+H)⁺.

Elementary Analysis as C₂₅H₂₂ClN₇O₇S₂ · 8.4H₂O.

Calculated : C,38.33; H,3.99; N,12.52; Cl,4.53; S,8.19 (%).

Found : C,37.89; H,3.62; N,12.41; Cl,4.41; S,7.93 (%).

Example 40



¹H-NMR (d₆-DMSO) δ : 1.37 (3H, d, J = 7.1 Hz), 2.96 and 3.26 (2H, ABq, J = 17.6 Hz), 4.02 (3H, s), 4.50 (2H, brs), 4.98 (1H, d, J = 4.8 Hz), 5.67 (1H, brs), 7.34 (1H, d, J = 3.0 Hz), 7.41 (2H, brs), 7.78 (1H, d, J = 6.0 Hz), 8.29 (1H, d, J = 3.0 Hz), 8.75 (1H, d, J = 7.9 Hz), 9.13 (1H, d, J = 6.0, 7.9 Hz), 9.75 (1H, brs).

IR (KBr) cm⁻¹: 3412, 1775, 1673, 1613, 1538, 1501, 1470, 1392, 1368, 1324, 1281, 1221, 1152, 1063, 1035..

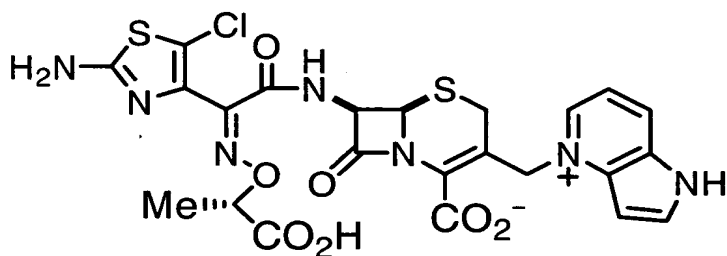
MS(ESI): 620⁺ (M+H)⁺ .

Elementary Analysis as C₂₃H₂₀ClN₇O₇S₂ · 2.1H₂O.

Calculated : C,42.90; H,3.79; N,15.23; Cl,5.51; S,9.96 (%).

Found : C,42.91; H,3.76; N,15.34; Cl,5.47; S,9.90 (%).

Example 41



¹H-NMR (d₆-DMSO) δ : 1.37 (3H, d, J = 7.1 Hz), 3.03 and 3.28 (2H, ABq, J = 17.4 Hz), 4.56 (1H, q, J = 7.1 Hz), 5.01 (1H, d, J = 4.8 Hz), 5.69 (3H, m), 7.32 (1H, d, J = 2.9 Hz), 7.41 (2H, s), 7.67 (1H, t-like), 8.27 (1H, d, J = 2.9 Hz), 8.60 (1H, d, J = 8.4 Hz), 9.06 (1H, d, J = 5.7 Hz), 9.68 (1H, brs), 13.45 (1H, brs).

IR (KBr) cm⁻¹: 3410, 2938, 1777, 1673, 1613, 1537, 1457, 1385, 1361, 1225, 1185, 1156, 1114, 1033.

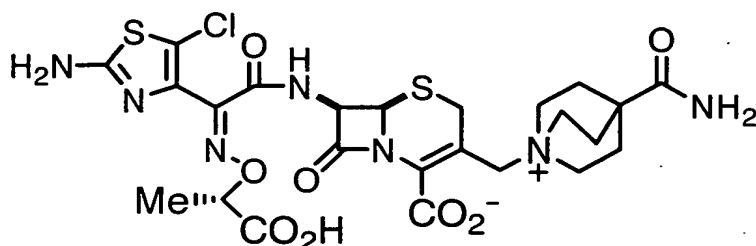
MS(ESI): 606⁺ (M+H)⁺ .

Elementary Analysis as C₂₃H₂₀ClN₇O₇S₂ · 2.5H₂O.

Calculated : C,42.43; H,3.87; N,15.06; Cl,5.45; S,9.85 (%).

Found : C,42.44; H,3.69; N,14.90; Cl,5.24; S,9.94 (%).

Example 42



¹H-NMR (D₂O) δ : 1.55 (3H, d, J = 7.1 Hz), 2.19 (6H, t-like), 3.39-3.56 (7H, m), 3.89 (1H, d, J = 16.8 Hz), 3.93 (1H, d, J = 13.9 Hz), 4.62 (1H, d, J = 13.9 Hz), 4.86 (1H, m), 5.36 (1H, d, J = 5.0 Hz),
5 5.90 (1H, d, J = 5.6 Hz).

IR (KBr) cm⁻¹: 3371, 1779, 1671, 1614, 1538, 1466, 1389, 1343, 1236, 1183, 1099, 1070, 1035.

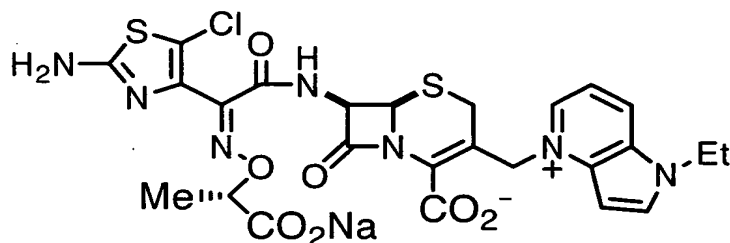
MS(ESI): 642⁺ (M+H)⁺.

Elementary Analysis as C₂₄H₂₈ClN₇O₈S₂ · 5.6H₂O.

10 Calculated : C,38.80; H,5.32; N,13.20; Cl,4.77; S,8.63 (%).

Found : C,38.57; H,4.76; N,13.24; Cl,4.56; S,8.32 (%).

Example 43



15 ¹H-NMR (d₆-DMSO) δ : 1.31 (3H, d, J = 7.1 Hz), 1.44 (3H, t, J = 7.2 Hz), 2.96 and 3.25 (2H, ABq, J = 17.1 Hz), 4.32 (1H, q, J = 7.1 Hz), 4.45 (2H, q, J = 7.2 Hz), 4.93 (1H, d, J = 5.1 Hz), 5.68 (2H, t-like), 5.75 (1H, dd, J = 5.1, 9.0 Hz), 7.31 (2H, s), 7.39 (1H, d, J = 3.5 Hz), 7.78 (1H, dd, J = 6.1, 8.1 Hz), 8.37 (1H, d, J = 3.5 Hz), 8.81 (1H, d, J = 8.1 Hz), 9.21 (1H, d, J = 6.1 Hz), 12.10 (1H, d, J = 9.0 Hz).

20 IR (KBr) cm⁻¹: 3409, 2982, 1772, 1604, 1539, 1496, 1460, 1394, 1362, 1317, 1289, 1230, 1185, 1153, 1106, 1033.

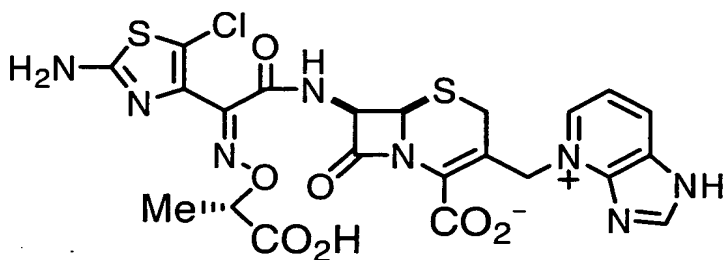
MS(ESI): 634⁺ (M+H)⁺.

Elementary Analysis as C₂₅H₂₃ClN₇N_aO₇S₂ · 3.7H₂O.

Calculated : C,41.55; H,4.24; N,13.57; Cl,4.91; S,8.87; Na,3.18 (%).

25 Found : C,41.48; H,3.96; N,13.60; Cl,4.84; S,8.87; Na, 3.26 (%).

Example 44



¹H-NMR (d₆-DMSO) δ : 1.35 (3H, d, J = 6.9 Hz), 3.12 and 3.49 (2H, ABq, J = 17.9 Hz), 4.54 (1H, q, J = 6.9 Hz), 5.12 (1H, d, J = 4.8 Hz), 5.57 and 5.68 (2H, ABq, J = 14.1 Hz), 5.81 (1H, dd, J = 4.8, 8.9 Hz), 7.42 (2H,s), 7.52 (1H, t-like), 8.55 (2H, brs), 8.71 (1H, d, J = 6.6 Hz), 9.54 (1H, d, J = 8.9 Hz).

IR (KBr) cm⁻¹: 3416, 1777, 1674, 1608, 1538, 1449, 1387, 1311, 1230, 1187, 1158, 1102, 1072, 1032.

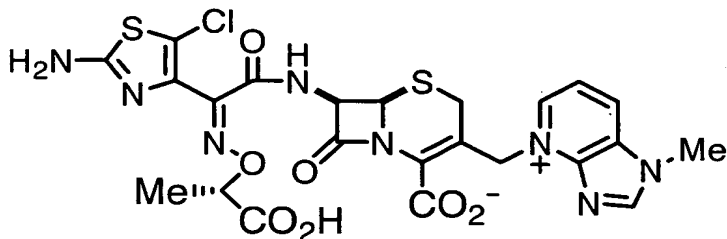
MS(ESI): 607⁺ (M+H)⁺.

Elementary Analysis as C₂₂H₁₉ClN₈O₇S₂ · 2.3H₂O.

Calculated : C,40.75; H,3.67; N,17.28; Cl,5.47; S,9.89 (%).

Found : C,40.72; H,3.55; N,17.35; Cl,5.51; S,9.90 (%).

Example 45



¹H-NMR (d₆-DMSO) δ : 1.34 (3H, d, J = 6.9 Hz), 3.00 and 3.51 (2H, ABq, J = 17.6 Hz), 4.07 (3H, s), 4.53 (1H, q, J = 6.9 Hz), 5.02 (1H, d, J = 5.4 Hz), 5.68-5.74 (3H, m), 7.41 (2H,s), 7.97 (1H, t-like), 8.89 (1H, d, J = 7.8 Hz), 9.04 (1H, s), 9.66 (2H, m).

IR (KBr) cm⁻¹: 3416, 1778, 1674, 1615, 1538, 1497, 1464, 1362, 1316, 1266, 1235, 1188, 1155, 1100, 1063, 1033.

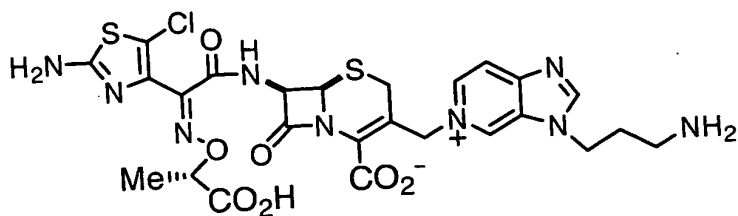
MS(ESI): 621⁺ (M+H)⁺.

Elementary Analysis as C₂₃H₂₁ClN₈O₇S₂ · 2.3H₂O.

Calculated : C,41.70; H,3.89; N,16.91; Cl,5.35; S,9.68 (%).

Found : C,41.67; H,3.85; N,16.90; Cl,5.27; S,9.60 (%).

Example 46



¹H-NMR (D₂O) δ : 1.43 (3H, d, J = 7.2 Hz), 2.35 (2H, m), 3.12 (2H, t-like), 3.19 and 3.68 (2H, ABq, J = 17.7 Hz), 4.61 (3H, q-like), 5.28 (1H, d, J = 5.1 Hz), 5.33 and 5.67 (2H, ABq, J = 14.7 Hz), 5.86 (1H, d, J = 5.1 Hz), 8.21 (1H, d, J = 6.3 Hz), 8.70 (1H, d, J = 6.3 Hz), 8.90 (1H, brs), 9.71

5 (1H, s).

IR (KBr) cm⁻¹: 3410, 1773, 1606, 1538, 1478, 1450, 1384, 1315, 1284, 1214, 1170, 1117, 1083, 1033..

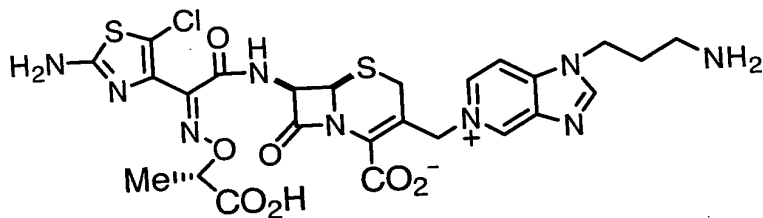
MS(ESI): 664⁺ (M+H)⁺.

Elementary Analysis as C₂₅H₂₆ClN₉O₇S₂ · 3.6H₂O.

10 Calculated : C,41.19; H,4.59; N,17.29; Cl,4.86; S,8.80(%).

Found : C,41.25; H,4.49; N,17.07; Cl,4.87; S,8.50 (%).

Example 47



15 ¹H-NMR (D₂O) δ : 1.42 (3H, d, J = 6.9 Hz), 2.34 (2H, m), 3.10 (2H, t-like), 3.18 and 3.63 (2H, ABq, J = 17.9 Hz), 4.55-4.67 (3H, m), 5.27(1H, d, J = 5.0 Hz), 5.35 and 5.66 (2H, ABq, J = 14.3 Hz), 5.87 (1H, d, J = 5.0 Hz), 8.22 (1H, d, J = 6.9 Hz), 8.79 (2H, d-like), 9.49 (1H, s).

IR (KBr) cm⁻¹: 3410, 1773, 1606, 1539, 1515, 1458, 1395, 1363, 1310, 1216, 1185, 1137, 1107, 1066, 1033.

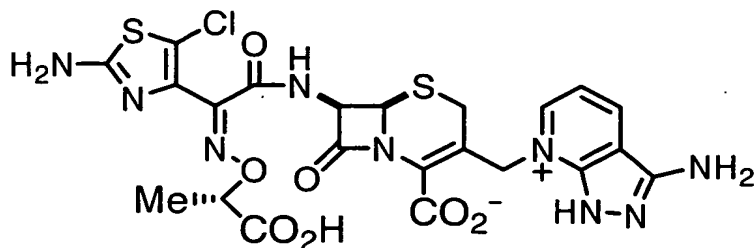
20 MS(ESI): 664⁺ (M+H)⁺.

Elementary Analysis as C₂₅H₂₆ClN₉O₇S₂ · 3.2H₂O.

Calculated : C,41.60; H,4.52; N,17.47; Cl,4.91; S,8.89 (%).

Found : C,41.63; H,4.48; N,17.40; Cl,4.82; S,8.73 (%).

25 Example 48



¹H-NMR (d₆-DMSO) δ : 1.34 (3H, d, J = 6.9 Hz), 2.84 and 3.51 (2H, ABq, J = 17.4 Hz), 4.51 (1H, q, J = 6.9 Hz), 5.11 (1H, d, J = 4.6 Hz), 5.14 and 5.54 (2H, ABq, J = 14.4 Hz), 5.72 (1H, dd, J = 4.6, 9.0 Hz), 6.59 (1H, brs), 7.34-7.40 (3H, m), 8.77 (2H, d, -like), 9.58 (1H, brs).

5 IR (KBr) cm⁻¹: 3414, 1774, 1638, 1574, 1538, 1446, 1391, 1367, 1334, 1227, 1182, 1078, 1036.

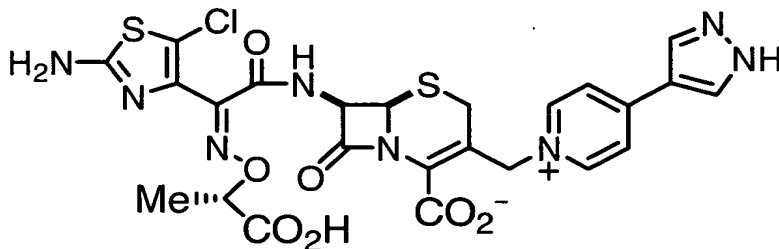
MS(ESI): 662⁺ (M+H)⁺.

Elementary Analysis as C₂₂H₂₀ClN₉O₇S₂ · 2.4H₂O.

Calculated : C,39.72; H,3.76; N,18.95; Cl,5.33; S,9.649 (%).

10 Found : C,39.77; H,3.69; N,19.04; Cl,5.27; S,9.49 (%).

Example 49



¹H-NMR (d₆-DMSO) δ : 1.37 (3H, d, J = 7.0 Hz), 3.09 and 3.51 (2H, ABq, J = 17.6 Hz), 4.54 (1H, q, J = 7.0 Hz), 4.99 and 5.51 (2H, ABq, J = 12.8 Hz), 5.70 (1H, dd, J = 4.7, 8.7 Hz), 7.42 (2H, s), 8.30 (2H, d, J = 6.5 Hz), 8.59 (2H, brs), 9.58 (1H, d, J = 8.7 Hz), 13.7 (1H, brs).

15 IR (KBr) cm⁻¹: 3314, 3194, 1777, 1671, 1637, 1570, 1538, 1470, 1391, 1344, 1285, 1221, 1156, 1100, 1065, 1034.

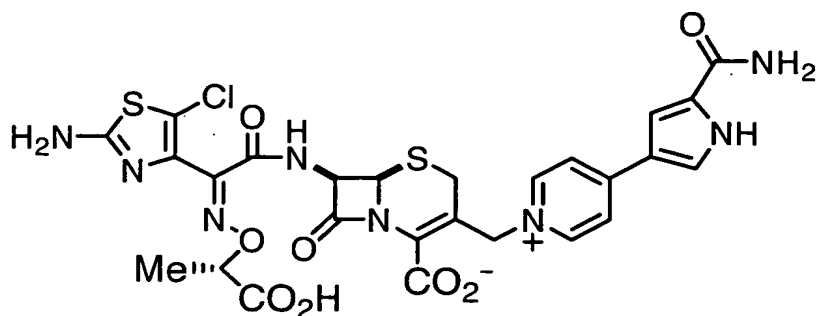
MS(ESI): 633⁺ (M+H)⁺.

20 Elementary Analysis as C₂₄H₂₁ClN₈O₇S₂ · 2.5H₂O.

Calculated : C,42.51; H,3.86; N,16.52; Cl,5.23; S,9.46 (%).

Found : C,42.44; H,3.67; N,16.68; Cl,5.36; S,9.36 (%).

Example 50



¹H-NMR (d₆-DMSO) δ : 1.37 (3H, d, J = 7.1 Hz), 3.09 and 3.51 (2H, ABq, J = 17.4 Hz), 4.76 (1H, q, J = 7.1 Hz), 4.94 and 5.49 (2H, ABq, J = 12.5 Hz), 5.07 (1H, d, J = 4.7 Hz), 5.72 (1H, dd, J = 4.7, 8.6 Hz), 7.27 (1H, brs), 7.41 (2H, s), 7.62 (1H, brs), 7.94 (1H, brs), 8.06 (1H, brs), 8.18 (2H, d, J = 5.9 Hz), 9.16 (2H, d, J = 5.9 Hz), 9.81 (1H, brs), 12.5 (1H, brs).

IR (KBr) cm⁻¹: 3402, 1775, 1718, 1636, 1608, 1570, 1550, 1441, 1393, 1343, 1288, 1220, 1150, 1035.

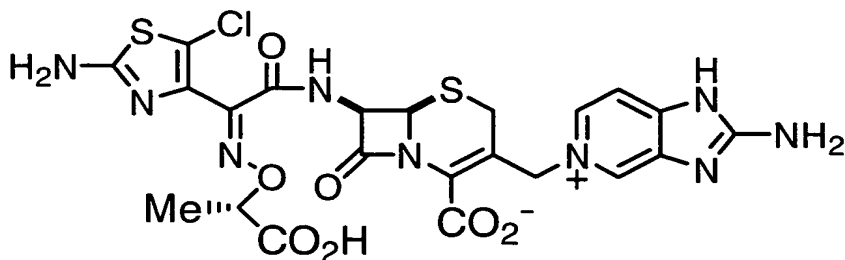
MS(ESI): 675⁺ (M+H)⁺.

Elementary Analysis as C₂₆H₂₃ClN₈O₈S₂ · 5.1H₂O.

Calculated : C,40.72; H,4.36; N,14.61; Cl,4.62; S,8.36 (%).

Found : C,40.56; H,3.97; N,14.44; Cl,5.09; S,8.05(%).

Example 51



¹H-NMR (d₆-DMSO) δ : 1.34 (3H, d, J = 7.0 Hz), 3.05 and 3.61 (2H, ABq, J = 17.9 Hz), 4.52 (1H, q, J = 7.0 Hz), 4.82 and 5.37 (2H, ABq, J = 14.4 Hz), 5.14 (1H, d, J = 5.0 Hz), 5.76 (1H, dd, J = 5.0, 8.9 Hz), 7.37 (2H, brs), 7.43 (1H, d, J = 6.9 Hz), 8.40 (2H, brs), 8.42 (1H, d, J = 6.9 Hz), 9.63 (2H, brs).

IR (KBr) cm⁻¹: 3336, 3192, 1774, 1662, 1617, 1573, 1539, 1489, 1393, 1332, 1246, 1188, 1153, 1119, 1066, 1034.

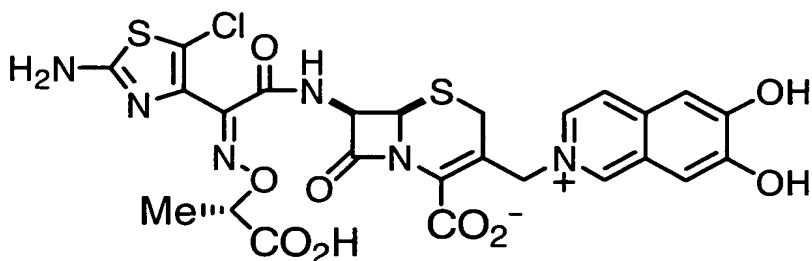
MS(ESI): 622⁺ (M+H)⁺.

Elementary Analysis as C₂₂H₂₀ClN₉O₇S₂ · 1.9H₂O.

Calculated : C,40.26; H,3.66; N,19.21; Cl,5.40; S,9.77 (%).

Found : C,40.48; H,3.69; N,19.26; Cl,5.10; S,9.48 (%).

Example 52



¹H-NMR (d₆-DMSO) δ : 1.37 (3H, d, J = 7.0 Hz), 3.18 and 3.52 (2H, ABq, J = 18.0 Hz), 4.56 (1H, q, J = 7.0 Hz), 5.11 (2H, m), 5.48 (1H, q, J = 13.8 Hz), 5.81 (1H, q, J = 4.7, 8.8 Hz), 7.12 (1H, rs), 7.41 (2H, s), 7.53 (1H, s), 7.83 (1H, d, J = 6.0 Hz), 8.38 (1H, d, J = 6.0 Hz), 9.24 (1H, brs), 9.63 (1H, d, J = 8.8 Hz).

IR (KBr) cm⁻¹: 3420, 1778, 1672, 1623, 1535, 1480, 1445, 1395, 1308, 1184, 1154, 1131, 1065, 1035.

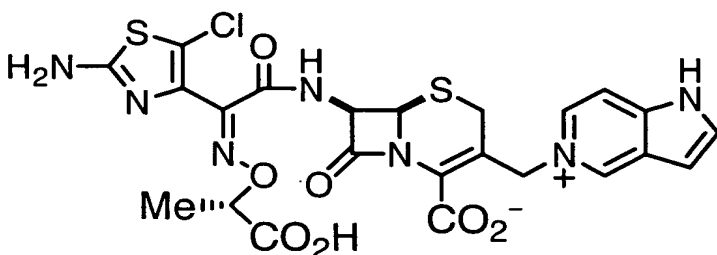
MS(ESI): 649⁺ (M+H)⁺.

Elementary Analysis as C₂₅H₂₁ClN₆O₉S₂ · 2.1H₂O.

Calculated : C,43.71; H,3.70; N,12.23; Cl,5.16; S,9.34 (%).

Found : C,44.06; H,3.69; N,12.31; Cl,5.00; S,9.94 (%).

Example 53



¹H-NMR (d₆-DMSO) δ : 1.35 (3H, d, J = 7.0 Hz), 3.04 and 3.50 (2H, ABq, J = 17.7 Hz), 4.54 (1H, q, J = 7.0 Hz), 5.08 (1H, d, J = 5.1 Hz), 5.15 and 5.65 (2H, ABq, J = 13.7 Hz), 5.73 (1H, dd, J = 5.1, 8.6 Hz), 7.01 (1H, d, J = 3.3 Hz), 7.42 (2H, s), 7.94 (1H, d, J = 3.3 Hz), 8.03 (1H, d, J = 6.6 Hz), 8.88 (1H, d, J = 6.6 Hz), 9.71 (1H, brs), 13.4 (1H, brs).

IR (KBr) cm⁻¹: 3395, 3009, 2937, 1777, 1673, 1632, 1537, 1484, 1445, 1378, 1359, 1227, 1187, 1153, 1117, 1065, 1034.

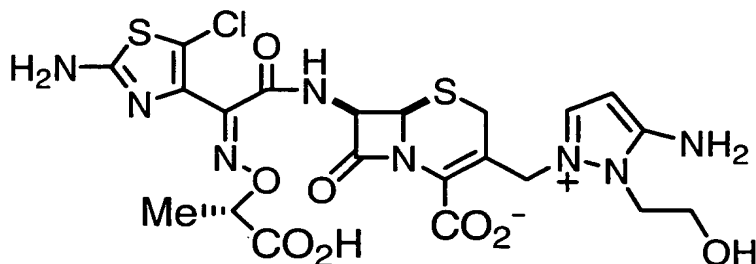
MS(ESI): 606⁺ (M+H)⁺.

Elementary Analysis as C₂₃H₂₀ClN₇O₇S₂ · 2.2H₂O.

Calculated : C,42.78; H,3.81; N,15.19; Cl,5.49; S,9.93 (%).

Found : C,42.87; H,3.81; N,15.20; Cl,5.30; S,9.86 (%).

Example 54



5

$^1\text{H-NMR}$ (d_6 -DMSO) δ : 1.41 (3H, d, J = 7.0 Hz), 2.97 and 3.21 (2H, ABq, J = 17.6 Hz), 3.58 (2H, brs), 4.58 (1H, q, J = 7.0 Hz), 5.06 (1H, d, J = 4.9 Hz), 5.10 and 5.23 (2H, ABq, J = 15.9 Hz), 5.70 (1H, dd, J = 4.9, 8.6 Hz), 5.83 (1H, d, J = 3.0 Hz), 7.26 (2H, s), 7.43 (2H, s), 8.08 (1H, d, J = 3.0Hz), 9.75 (1H, brs).

10 IR (KBr) cm^{-1} : 3411, 2939, 1775, 1635, 1537, 1456, 1325, 1221, 1151, 1097, 1036.

MS(ESI): 615 $^+$ ($\text{M}+\text{H}$) $^+$.

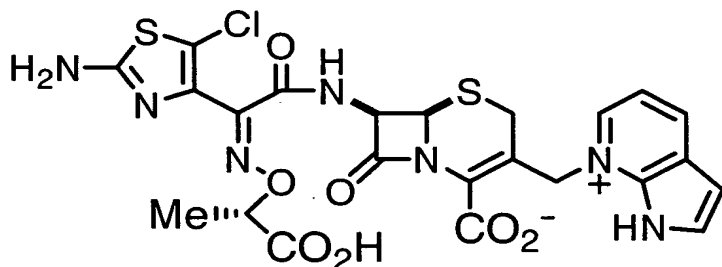
Elementary Analysis as $\text{C}_{21}\text{H}_{23}\text{ClN}_8\text{O}_8\text{S}_2 \cdot 2.6\text{H}_2\text{O}$.

Calculated : C,38.11; H,4.29; N,16.93; Cl,5.36; S,9.69 (%).

Found : C,38.04; H,3.93; N,16.67; Cl,5.49; S,9.68 (%).

15

Example 55



$^1\text{H-NMR}$ (d_6 -DMSO) δ : 1.30 (3H, d, J = 7.0 Hz), 2.76 and 3.57 (2H, ABq, J = 18.0 Hz), 4.48 (1H, q, J = 7.0 Hz), 5.13 (1H, d, J = 4.9 Hz), 5.24 and 5.90 (2H, ABq, J = 14.3 Hz), 5.72 (1H, dd, J = 4.9, 8.4 Hz), 6.89 (1H, d, J = 3.3 Hz), 7.40 (2H, s), 7.58 (1H, dd, J = 6.0, 7.8 Hz), 7.92 (1H, d, J = 3.3 Hz), 8.71 (2H, m), 9.54 (1H, d, J = 8.4 Hz).

20

IR (KBr) cm^{-1} : 3413, 2934, 2718, 1777, 1675, 1616, 1537, 1480, 1461, 1362, 1230, 1189, 1112, 1034.

MS(ESI): 606 $^+$ ($\text{M}+\text{H}$) $^+$.

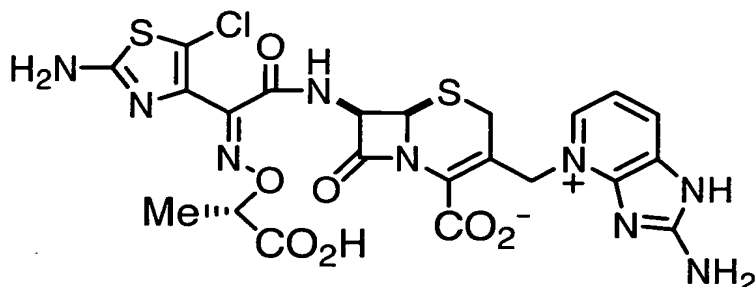
25

Elementary Analysis as $\text{C}_{23}\text{H}_{20}\text{ClN}_7\text{O}_7\text{S}_2 \cdot 2.3\text{H}_2\text{O}$.

Calculated : C,42.67; H,3.83; N,15.14; Cl,5.48; S,9.90 (%).

Found : C,42.65; H,3.82; N,15.18; Cl,5.40; S,9.74 (%).

Example 56



5

$^1\text{H-NMR}$ ($\text{d}_6\text{-DMSO}$) δ : 1.39 (3H, d, J = 7.1 Hz), 3.15 and 3.52 (2H, ABq, J = 17.7 Hz), 4.56 (1H, q, J = 7.1 Hz), 5.10 (1H, d, J = 4.9 Hz), 5.36 (2H, brs), 5.80 (1H, dd, J = 4.9, 8.6 Hz), 7.11 (1H, t, J = 7.2 Hz), 7.69 (1H, d, J = 7.2 Hz), 8.42 (3H, m), 9.84 (1H, brs).

IR (KBr) cm^{-1} : 3352, 3151, 2712, 1772, 1665, 1607, 1583, 1543, 1490, 1443, 1408, 1390, 1368, 1341, 1300, 1211, 1160, 1106, 1083, 1060, 1031.

10

MS(ESI): 622 $^+$ ($\text{M}+\text{H}$) $^+$.

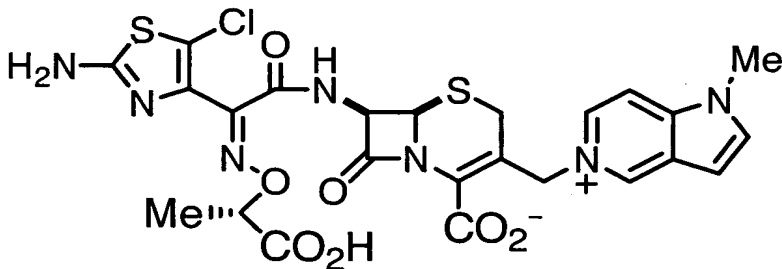
Elementary Analysis as $\text{C}_{22}\text{H}_{20}\text{ClN}_9\text{O}_7\text{S}_2 \cdot 3.0\text{H}_2\text{O}$.

Calculated : C,39.08; H,3.88; N,18.65; Cl,5.24; S,9.49 (%).

Found : C,39.26; H,3.83; N,18.75; Cl,5.33; S,9.19 (%).

15

Example 57



$^1\text{H-NMR}$ ($\text{d}_6\text{-DMSO}$) δ : 1.34 (3H, d, J = 6.9 Hz), 2.97 and 3.48 (2H, ABq, J = 17.6 Hz), 3.98 (3H, s), 4.52 (1H, q, J = 6.9 Hz), 5.05-5.12 (2H, m), 5.63-5.72 (2H, m), 7.09 (1H, d, J = 3.1 Hz), 7.42 (2H, s), 7.94 (1H, d, J = 3.1 Hz), 8.17 (1H, d, J = 7.1 Hz), 9.49 (1H, d, J = 7.1 Hz), 9.64 (1H, brs), 9.7 (1H, brs).

20

IR (KBr) cm^{-1} : 3406, 3073, 2945, 1778, 1675, 1631, 1538, 1447, 1361, 1324, 1254, 1227, 1184, 1132, 1106, 1065, 1033.

MS(FAB): 620 ($\text{M}+\text{H}$) $^+$.

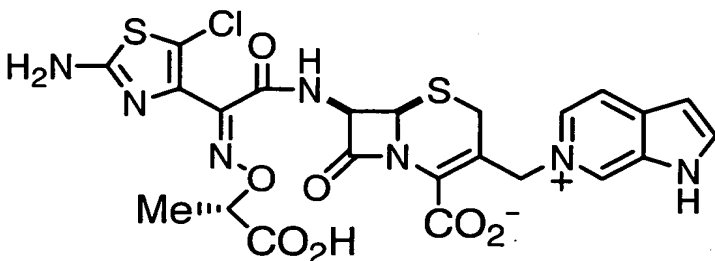
25

Elementary Analysis as $\text{C}_{24}\text{H}_{22}\text{ClN}_7\text{O}_7\text{S}_2 \cdot 2.4\text{H}_2\text{O}$.

Calculated : C,43.46; H,4.07; N,14.78; Cl,5.34; S,9.67 (%).

Found : C,43.45; H,4.03; N,14.88; Cl,5.25; S,9.55 (%).

Example 58



5

¹H-NMR (d₆-DMSO) δ : 1.35 (3H, d, J = 6.9 Hz), 3.04 and 3.56 (2H, ABq, J = 17.6 Hz), 4.53 (1H, q, J = 7.0 Hz), 5.09-5.15 (2H, m), 5.68-5.76 (2H, m), 6.92 (1H, d, J = 2.7 Hz), 7.40 (2H, s), 8.11 (1H, d, J = 6.9 Hz), 8.30 (1H, d, J = 2.7 Hz), 8.55 (1H, d, J = 6.9 Hz), 9.84 (2H, brs), 14.7 (1H, brs).

IR (KBr) cm⁻¹: 3326, 3195, 2938, 1777, 1674, 1612, 1537, 1461, 1375, 1312, 1234, 1187,

10 1145, 1065, 1034.

MS(ESI): 606 (M+H)⁺.

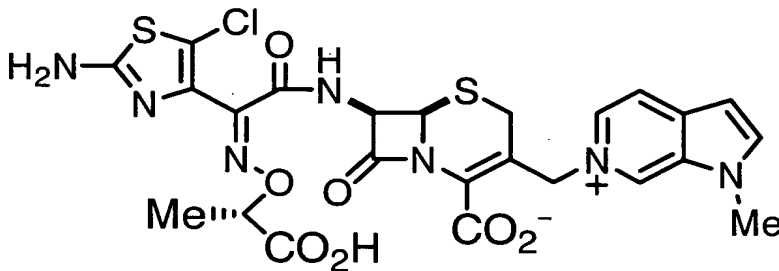
Elementary Analysis as C₂₃H₂₀ClN₇O₇S₂ · 2.5H₂O.

Calculated : C,42.43; H,3.87; N,15.06 Cl,5.45; S,9.85 (%).

Found : C,42.46; H,3.74; N,15.01; Cl,5.33; S,9.93 (%).

15

Example 59



¹H-NMR (d₆-DMSO) δ : 1.34 (3H, d, J = 7.0 Hz), 3.08 and 3.49 (2H, ABq, J = 17.6 Hz), 4.04 (3H, s), 4.52 (1H, q, J = 7.0 Hz), 5.05-5.12 (2H, m), 5.66-5.72 (2H, m), 6.92 (1H, d, J = 2.9 Hz), 7.42 (2H, brs), 8.14 (1H, d, J = 6.8 Hz), 8.28 (1H, d, J = 2.9 Hz), 8.97 (1H, d, J = 6.8 Hz), 9.64 (1H, brs), 9.80 (1H, brs).

20

IR (KBr) cm⁻¹: 3410, 1777, 1676, 1614, 1537, 1486, 1447, 1423, 1378, 1326, 1260, 1230,

1161, 1096, 1065, 1033.

MS(ESI): 620 (M+H)⁺.

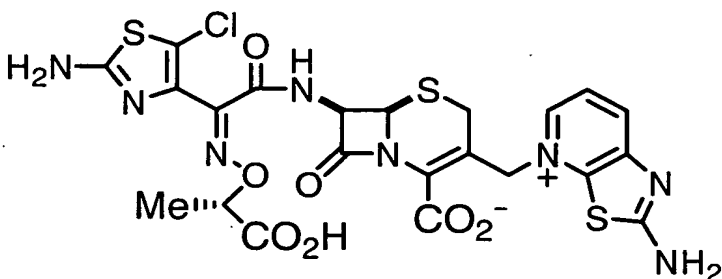
25

Elementary Analysis as C₂₄H₂₂ClN₇O₇S₂ · 2.4H₂O.

Calculated : C,43.46; H,4.07; N,14.78; Cl,5.34; S,9.67 (%).

Found : C,43.47; H,3.97; N,14.79; Cl,5.21; S,9.59 (%).

Example 60



5

¹H-NMR (d₆-DMSO) δ : 1.39 (3H, d, J = 7.1 Hz), 3.15 and 3.34 (2H, ABq, J = 17.6 Hz), 4.56 (1H, q, J = 7.1 Hz), 5.05 (1H, d, J = 4.8 Hz), 5.47 (1H, d, J = 14.1 Hz), 5.72-5.78 (2H,m), 7.41 (2H, brs), 7.84 (1H, dd, J = 5.9, 8.1 Hz), 8.21 (1H, d, J = 8.1 Hz), 8.83 (1H, d, J = 5.9 Hz), 8.89 (2H, brs), 9.87 (1H, brs).

10 IR (KBr) cm⁻¹: 3312, 3189, 1778, 1630, 1537, 1426, 1386, 1341, 1308, 1214, 1186, 1129, 1064, 1034.

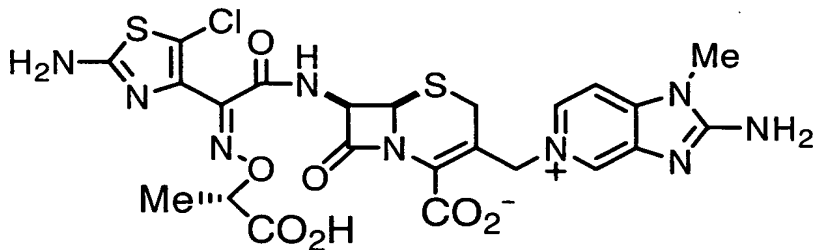
MS(FAB): 639⁺ (M+H)⁺.

Elementary Analysis as C₂₂H₁₉ClN₈O₇S₃ · 3.2H₂O.

Calculated : C,37.92; H,3.67; N,16.08; Cl,5.09; S,13.81(%).

15 Found : C,37.95; H,3.60; N,16.04; Cl,5.07; S,13.60 (%).

Example 61



20 ¹H-NMR (d₆-DMSO) δ : 1.35 (3H, d, J = 7.0 Hz), 2.90 and 3.46 (2H, ABq, J = 17.6 Hz), 3.66 (3H, s), 4.53 (1H, q, J = 7.0 Hz), 4.96 and 5.56 (2H, ABq, J = 13.7 Hz), 5.06 (1H, d, J = 4.9 Hz), 5.69 (1H, dd, J = 4.9, 8.9 Hz), 7.42 (2H, brs), 7.73 (2H, brs), 7.81 (1H, d, J = 6.6 Hz), 8.81 (1H, d, J = 6.6 Hz), 9.63 (1H, brs).

IR (KBr) cm⁻¹: 3346, 3180, 1775, 1664, 1613, 1567, 1538, 1508, 1448, 1389, 1352, 1311, 1271, 1179, 1100, 1065, 1034.

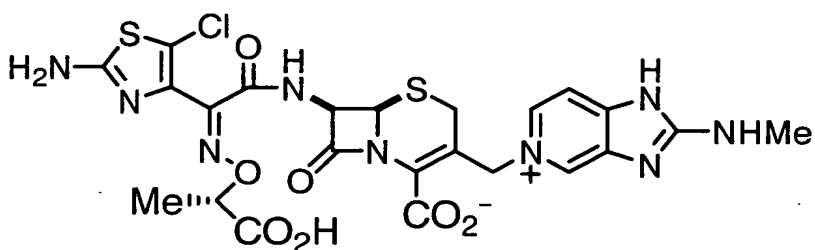
25 MS(FAB): 636⁺ (M+H)⁺.

Elementary Analysis as C₂₃H₂₂ClN₉O₇S₂ · 2.7H₂O.

Calculated : C,40.35; H,4.03; N,18.41; Cl,5.18; S,9.37 (%).

Found : C,40.32; H,3.90; N,18.39; Cl,5.14; S,9.35 (%).

Example 62



¹H-NMR (d₆-DMSO) δ : 1.35 (3H, d, J = 7.0 Hz), 3.03–3.09 (4H, m), 3.61 (1H, d, J = 18.0 Hz), 4.52 (1H, q, J = 7.0 Hz), 4.83 and 5.40 (2H, ABq, J = 14.0 Hz), 5.14 (1H, d, J = 5.0 Hz), 5.77 (1H, dd, J = 5.0, 8.7 Hz), 7.36 (2H, brs), 7.48 (1H, d, J = 6.8 Hz), 8.43 (1H, d, J = 6.8 Hz), 9.33 (1H, brs), 9.59 (1H, brs), 9.70 (1H, brs).

IR (KBr) cm⁻¹: 3370, 1775, 1644, 1579, 1538, 1479, 1394, 1329, 1239, 1188, 1121, 1066, 1034.

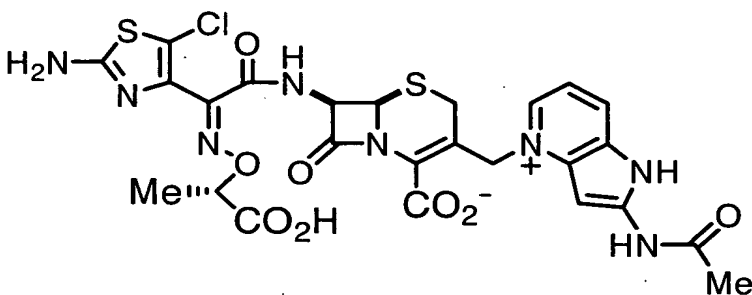
MS(FAB): 636⁺ (M+H)⁺.

Elementary Analysis as C₂₃H₂₂ClN₉O₇S₂ · 2.2H₂O.

Calculated : C,40.88; H,3.94; N,18.66; Cl,5.25; S,9.49 (%).

Found : C,41.07; H,4.21; N,18.30; Cl,4.86; S,8.86 (%).

Example 63



¹H-NMR (d₆-DMSO) δ : 1.41 (3H, d, J = 7.0 Hz), 2.16 (3H, s), 3.10 (1H, d, J = 17.1 Hz), 4.59 (1H, q, J = 7.0 Hz), 5.08 (1H, d, J = 5.1 Hz), 5.51 (2H, brs), 5.76 (1H, dd, J = 5.1, 8.4 Hz), 6.87 (1H, s), 7.33 (1H, t-like), 7.39 (2H, brs), 8.01 (1H, brs), 8.59 (1H, d, J = 6.0 Hz), 9.70 (1H, brs), 12.7 (1H, brs).

IR (KBr) cm⁻¹: 3325, 1776, 1653, 1609, 1561, 1470, 1416, 1369, 1352, 1236, 1183, 1158, 1100, 1065, 1032.

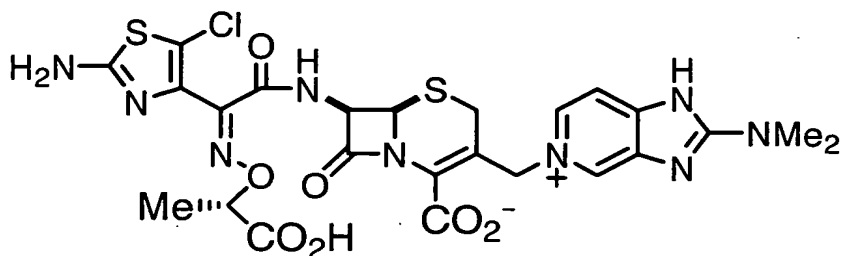
MS(FAB): 663⁺ (M+H)⁺.

Elementary Analysis as C₂₅H₂₃ClN₈O₈S₂ · 3.2H₂O.

Calculated : C,41.66; H,4.11; N,15.55; Cl,4.92; S,8.90 (%).

Found : C,41.79; H,4.14; N,15.37; Cl,4.82; S,8.75 (%).

Example 64



5

$^1\text{H-NMR}$ (d_6 -DMSO) δ : 1.36 (3H, d, J = 7.1 Hz), 2.98 and 3.50 (2H, ABq, J = 17.3 Hz), 3.21 (6H,s), 4.54 (1H, q, J = 7.1 Hz), 5.00 and 5.48 (2H, ABq, J = 13.5 Hz), 5.16 (1H, d, J = 4.8 Hz), 5.72 (1H, dd, J = 4.8, 9.0 Hz), 7.39 (2H, brs), 7.49 (1H, d, J = 6.9 Hz), 8.44 (1H, d, J = 6.9 Hz), 9.09 (1H, brs), 9.85 (1H, brs).

10 IR (KBr) cm^{-1} : 3413, 2938, 1777, 1639, 1557, 1538, 1440, 1391, 1335, 1247, 1190, 1150, 1121, 1065, 1034.

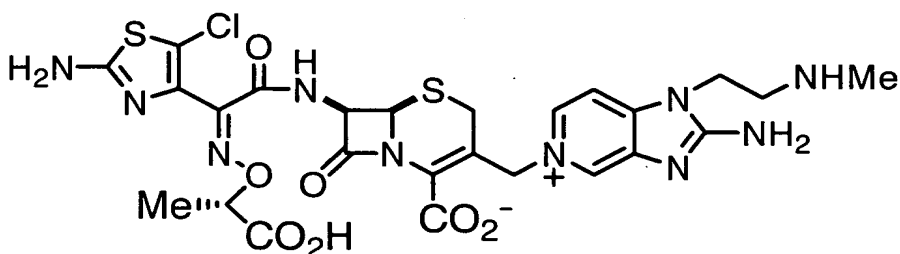
MS(FAB): 650⁺ (M+H)⁺.

Elementary Analysis as $\text{C}_{24}\text{H}_{24}\text{ClN}_9\text{O}_7\text{S}_2 \cdot 3.2\text{H}_2\text{O}$.

Calculated : C,40.73; H,4.33; N,17.81; Cl,5.01; S,9.06 (%).

15 Found : C,40.73; H,4.24; N,17.75; Cl,5.08; S,9.10 (%).

Example 65



20 $^1\text{H-NMR}$ ($\text{D}_2\text{O} + \text{DCl}$) δ : 1.55 (3H, d, J = 7.1 Hz), 2.82 (3H, s), 3.36 and 3.75 (2H, ABq, J = 18.5 Hz), 4.72 (2H, t, J = 6.5 Hz), 4.99 (1H, q, J = 7.1 Hz), 5.36 (1H, d, J = 4.8 Hz), 5.40 and 5.86 (2H, ABq, J = 14.9 Hz), 5.94 (1H, d, J = 4.8 Hz), 8.09 (1H, d, J = 6.8 Hz), 8.83 (1H, d, J = 6.8 Hz), 9.06 (1H, s).

IR (KBr) cm^{-1} : 3370, 3174, 1771, 1667, 1606, 1541, 1504, 1449, 1399, 1360, 1312, 1281, 1184, 1113, 1067, 1035.

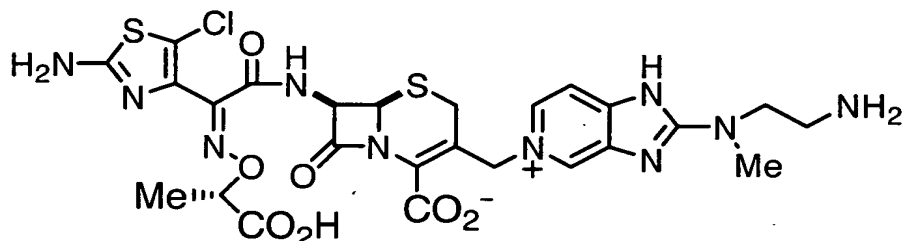
25 MS(FAB): 679⁺ (M+H)⁺.

Elementary Analysis as $C_{25}H_{27}ClN_{10}O_7S_2 \cdot 4.0H_2O$.

Calculated : C,39.97; H,4.70; N,18.65; Cl,4.72; S,8.54 (%).

Found : C,40.02; H,4.64; N,18.79; Cl,4.60; S,8.31 (%).

5 Example 66



1H -NMR ($D_2O + DCl$) δ : 1.55 (3H, d, $J = 7.1$ Hz), 3.29–3.45 (6H, m), 3.69 (1H, d, $J = 18.3$ Hz), 4.04 (2H, t, $J = 6.2$ Hz), 4.98 (1H, q, $J = 7.1$ Hz), 5.28–5.35 (2H, m), 5.70 (1H, s), 5.93 (1H, d, $J = 4.8$ Hz), 7.68 (1H, d, $J = 4.6$ Hz), 8.45 (1H, dd, $J = 1.2, 4.6$ Hz), 8.73 (1H, d, $J = 1.2$ Hz).

10 IR (KBr) cm^{-1} : 3397, 1772, 1623, 1578, 1540, 1508, 1446, 1397, 1330, 1247, 1190, 1151, 1121, 1066, 1034.

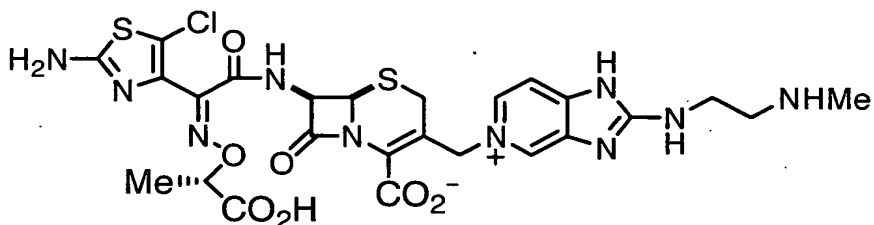
MS(FAB): 679⁺ ($M+H$)⁺.

Elementary Analysis as $C_{25}H_{27}ClN_{10}O_7S_2 \cdot 4.3H_2O$.

Calculated : C,39.69; H,4.74; N,18.51; Cl,4.69; S,8.48 (%).

15 Found : C,39.77; H,4.70; N,18.43; Cl,4.59; S,8.48 (%).

Example 67



1H -NMR ($D_2O + DCl$) δ : 1.54 (3H, d, $J = 7.1$ Hz), 2.80 (3H, s), 3.29 and 3.66 (2H, ABq, $J = 18.3$ Hz), 3.41 (2H, t, $J = 5.8$ Hz), 3.89 (2H, t, $J = 5.8$ Hz), 4.96 (1H, q, $J = 7.1$ Hz), 5.27–5.33 (2H, m), 5.61 (1H, d, $J = 14.8$ Hz), 5.93 (1H, d, $J = 4.8$ Hz), 7.67 (1H, d, $J = 6.8$ Hz), 8.43 (1H, d, $J = 6.8$ Hz), 8.71 (1H, s).

IR (KBr) cm^{-1} : 3388, 1773, 1626, 1540, 1477, 1395, 1361, 1238, 1186, 1152, 1120, 1065, 1035.

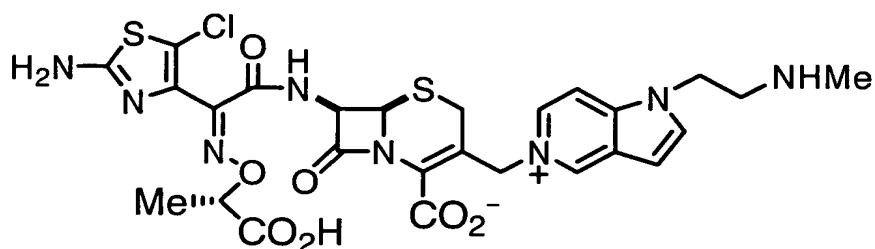
25 MS(FAB): 679⁺ ($M+H$)⁺.

Elementary Analysis as $C_{25}H_{27}ClN_{10}O_7S_2 \cdot 3.7H_2O$.

Calculated : C,40.26; H,4.65; N,18.78; Cl,4.75; S,8.60 (%).

Found : C,40.23; H,4.60; N,18.76; Cl,4.79; S,8.51 (%).

Example 68



¹H-NMR (D₂O) δ : 1.42 (3H, d, J = 6.9 Hz), 2.74 (3H, s), 3.17 (1H, d, J = 18.0 Hz), 3.56-3.61 (3H, m), 4.61-4.76 (3H, m), 5.23-5.31 (2H, m), 5.54 (1H, d, J = 14.7 Hz), 5.56 (1H, d, J = 4.5 Hz), 7.12 (1H, d, J = 3.4 Hz), 7.80 (1H, d, J = 3.4 Hz), 7.99 (1H, d, J = 7.0 Hz), 8.52 (1H, d, J = 7.0 Hz), 9.086 (1H, s).

IR (KBr) cm⁻¹: 3398, 2452, 1773, 1604, 1540, 1514, 1494, 1448, 1395, 1363, 1286, 1223,

1187, 1119, 1065, 1034.

MS(FAB): 663⁺ (M+H)⁺.

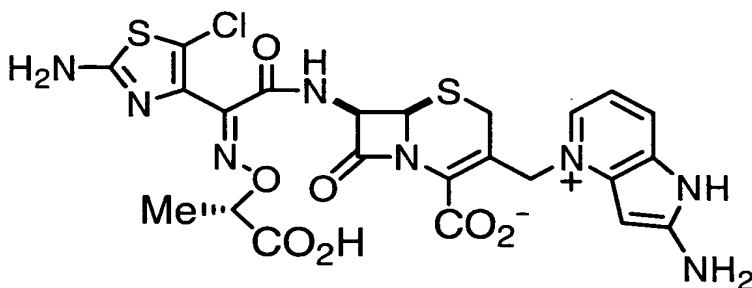
Elementary Analysis as C₂₆H₂₇ClN₈O₇S₂ · 4.0H₂O.

Calculated : C,42.48; H,4.80; N,15.24; Cl,4.82; S,8.72 (%).

Found : C,42.45; H,4.57; N,15.20; Cl,4.86; S,8.70 (%).

15

Example 69



¹H-NMR (d₆-DMSO) δ : 1.39 (3H, d, J = 7.0 Hz), 3.02 and 3.31 (2H ABq, J = 17.7 Hz), 4.57 (1H, q, J = 7.0 Hz), 5.05 (1H, d, J = 4.9 Hz), 5.22 and 5.35 (2H, ABq, J = 14.4 Hz), 5.75 (1H, dd, J = 4.9, 9.0 Hz), 5.87 (1H, s), 6.84 (1H, t-like), 7.39 (2H, brs), 7.49 (1H, d, J = 7.5 Hz), 7.82 (1H, brs), 8.09 (1H, d, J = 6.6 Hz), 9.86 (1H, brs), 12.9 (1H, brs).

IR (KBr) cm⁻¹: 3338, 3198, 1773, 1640, 1581, 1540, 1497, 1427, 1364, 1329, 1285, 1239,

1192, 1159, 1099, 1034.

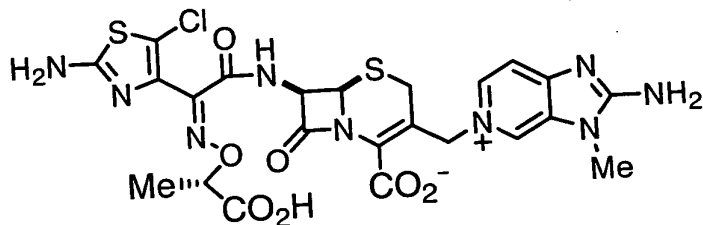
MS(FAB): 621⁺ (M+H)⁺.

25 Elementary Analysis as C₂₃H₂₁ClN₈O₇S₂ · 2.9H₂O.

Calculated : C,41.03; H,4.01; N,16.64; Cl,5.27; S,9.52 (%).

Found : C,41.01; H,3.90; N,16.64; Cl,5.37; S,9.49 (%).

Example 70



5 ¹H-NMR (d₆-DMSO) δ : 1.36 (3H, d, J = 7.1 Hz), 3.01 and 3.47 (2H, ABq, J = 17.7 Hz), 3.60 (3H, s), 4.53 (1H, q, J = 7.1 Hz), 4.90 and 5.50 (2H, ABq, J = 13.7 Hz), 5.04 (1H, d, J = 4.9 Hz), 5.69 (1H, dd, J = 4.9, 9.0 Hz), 7.40 (2H, brs), 7.51 (1H, d, J = 6.8 Hz), 8.14 (2H, brs), 8.82 (1H, d, J = 6.8 Hz), 9.13 (1H, brs), 9.68 (1H, brs).

IR (KBr) cm⁻¹: 3354, 3190, 1774, 1658, 1557, 1485, 1467, 1389, 1347, 1231, 1162, 1094,

10 1066, 1035.

MS(FAB): 636⁺ (M+H)⁺.

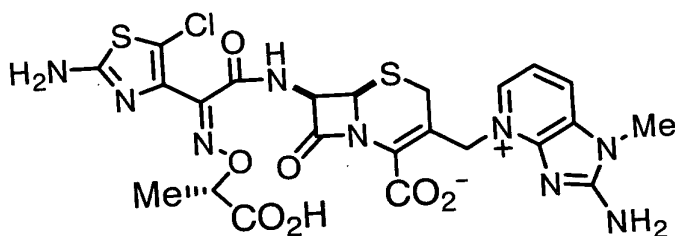
Elementary Analysis as C₂₃H₂₂ClN₉O₇S₂ · 3.2H₂O.

Calculated : C,39.82; H,4.13; N,18.17; Cl,5.11; S,9.24 (%).

Found : C,39.85; H,4.07; N,18.08; Cl,5.02; S,9.12 (%).

15

Example 71



20 ¹H-NMR (D₂O + DCl) δ : 1.54 (3H, d, J = 7.2 Hz), 3.33 and 3.59 (2H ABq, J = 18.5 Hz), 3.67 (3H, s), 4.99 (1H, q, J = 7.2 Hz), 5.29 (1H, d, J = 4.8 Hz), 5.22 and 5.65 (2H, ABq, J = 15.2 Hz), 5.91 (1H, d, J = 4.8 Hz), 7.33 (1H, dd, J = 6.5, 7.8 Hz), 7.91 (1H, d, J = 7.8 Hz), 8.10 (1H, d, J = 6.5 Hz).

IR (KBr) cm⁻¹: 3455, 3351, 3288, 3041, 2949, 2899, 1746, 1699, 1671, 1651, 1625, 1606, 1579, 1533, 1494, 1462, 1447, 1422, 1404, 1364, 1354, 1303, 1275, 1254, 1227, 1209, 1189, 1173, 1155, 1140, 1091, 1076, 1064, 1026.

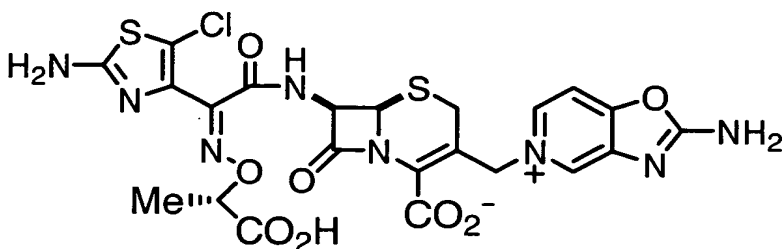
MS(FAB): 636⁺ (M+H)⁺.

25 Elementary Analysis as C₂₃H₂₂ClN₉O₇S₂ · 2.5H₂O.

Calculated : C,42.82; H,3.59; N,19.54; Cl,5.50; S,9.94 (%).

Found : C,42.84; H,3.55; N,19.51; Cl,5.43; S,10.00 (%).

Example 72



¹H-NMR (d₆-DMSO) δ : 1.37 (3H, d, J = 7.1 Hz), 3.00 and 3.49 (2H, ABq, J = 17.7 Hz), 4.54 (1H, q, J = 7.1 Hz), 5.02 and 5.63 (2H, ABq, J = 13.7 Hz), 5.07 (1H, d, J = 5.0 Hz), 5.72 (1H, dd, J = 5.0, 8.7 Hz), 7.41 (2H, brs), 8.12 (1H, d, J = 7.1 Hz), 8.72 (2H, brs), 9.10 (1H, d, J = 7.1 Hz), 9.45 (1H, brs), 9.55 (1H, d, J = 8.7 Hz).

IR (KBr) cm⁻¹: 3385, 1776, 1692, 1617, 1538, 1492, 1363, 1287, 1223, 1188, 1150, 1103,

1066, 1036.

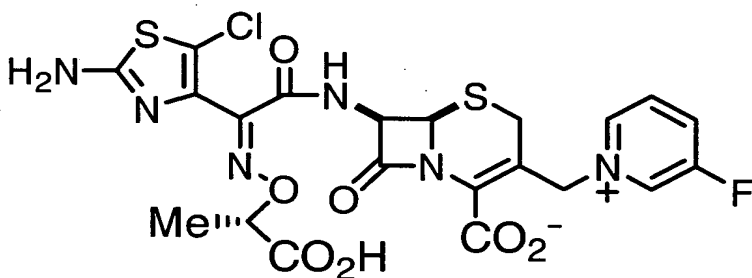
MS(FAB): 623⁺ (M+H)⁺.

Elementary Analysis as C₂₂H₁₉ClN₈O₈S₂ · 2.9H₂O.

Calculated : C,39.13; H,3.70; N,16.59; Cl,5.25; S,9.50 (%).

Found : C,39.04; H,3.55; N,16.69; Cl,5.12; S,9.52 (%).

Example 73



¹H-NMR (d₆-DMSO) δ : 1.38 (3H, d, J = 7.0 Hz), 3.15 and 3.50 (2H, ABq, J = 17.6 Hz), 4.55 (1H, q, J = 7.0 Hz), 5.07 (1H, d, J = 5.1 Hz), 5.11 (1H, d, J = 13.2 Hz), 5.65-5.74 (2H, m), 7.41 (2H, brs), 8.24-8.31 (1H, m), 8.62-8.68 (1H, m), 9.46 (1H, d, J = 6.0 Hz), 9.52 (1H, d, J = 8.7 Hz), 9.89 (1H, brs).

IR (KBr) cm⁻¹: 3411, 3068, 2943, 1778, 1673, 1616, 1538, 1503, 1446, 1390, 1345, 1275, 1189, 1137, 1097, 1065, 1035.

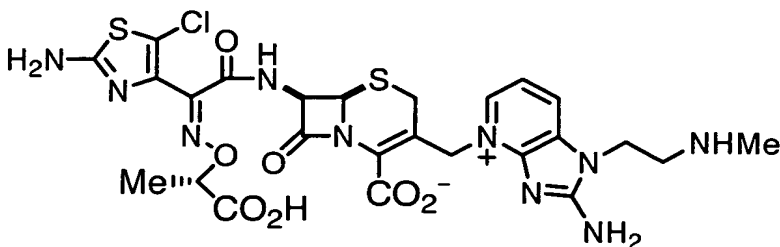
MS(FAB): 585⁺ (M+H)⁺.

Elementary Analysis as C₂₁H₁₈ClFN₆O₇S₂ · 2.9H₂O.

Calculated : C,39.58; H,3.76; N,13.19; Cl,5.56; S,10.06 (%).

Found : C,39.52; H,3.59; N,13.24; Cl,5.65; S,10.25 (%).

Example 74



¹H-NMR (D₂O + DCl) δ : 1.54 (3H, d, J = 7.1 Hz), 2.78 (3H, s), 3.37 (1H, d, J = 18.3 Hz), 3.54-3.62 (3H, m), 4.57 (2H, t, J = 6.5 Hz), 4.98 (1H, q, J = 7.1 Hz), 5.27 (1H, d, J = 4.8 Hz), 5.49 and 5.71 (2H, ABq, J = 15.2 Hz), 5.91 (1H, d, J = 4.8 Hz), 7.34 (1H, t-like), 8.00 (1H, d, J = 7.8 Hz), 8.17 (1H, d, J = 6.6 Hz).

IR (KBr) cm⁻¹: 3398, 2451, 1771, 1666, 1603, 1562, 1493, 1396, 1362, 1315, 1387, 1224, 1165, 1090, 1034.

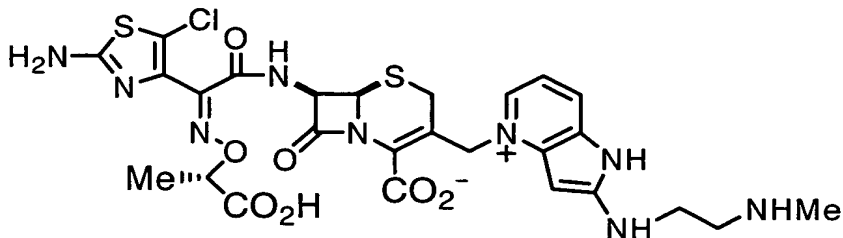
MS(FAB): 679⁺ (M+H)⁺.

Elementary Analysis as C₂₅H₂₇ClN₁₀O₇S₂ · 3.6H₂O.

Calculated : C,40.36; H,4.63; N,18.83; Cl,4.77; S,8.62 (%).

Found : C,40.32; H,4.68; N,18.84; Cl,4.87; S,8.77 (%).

Example 75



¹H-NMR (D₂O + DCl) δ : 1.54 (3H, d, J = 7.1 Hz), 2.64 (3H, s), 3.25 and 3.45 (2H ABq, J = 18.3 Hz), 3.38 (2H, t, J = 5.9 Hz), 3.76 (2H, t, J = 5.9 Hz), 4.98 (1H, q, J = 7.1 Hz), 5.26 (1H, d, J = 4.8 Hz), 5.39 and 5.48 (2H, ABq, J = 15.5 Hz), 5.89 (1H, d, J = 4.8 Hz), 7.10 (1H, t-like), 7.73 (1H, d, J = 7.8 Hz), 7.94 (1H, d, J = 6.6 Hz).

IR (KBr) cm⁻¹: 3389, 1771, 1590, 1540, 1428, 1395, 1360, 1317, 1284, 1192, 1158, 1113, 1058, 1033.

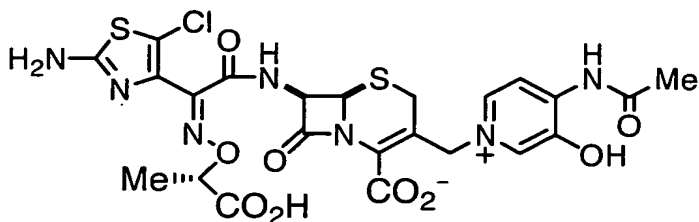
MS(FAB): 678⁺ (M+H)⁺.

Elementary Analysis as C₂₆H₂₈ClN₉O₇S₂ · 3.3H₂O.

Calculated : C,42.34; H,4.73; N,17.09; Cl,4.81; S,8.69 (%).

Found : C,42.11; H,4.67; N,17.00; Cl,4.94; S,9.09 (%).

Example 76



¹H-NMR (d₆-DMSO) δ : 1.40 (3H, d, J = 7.1 Hz), 2.26 (3H,s), 3.12 and 3.45 (2H, ABq, J = 17.7 Hz), 4.59 (1H, q, J = 7.1 Hz), 5.20 (1H, d, J = 4.9 Hz), 5.78 (1H, dd, J = 4.9, 9.2 Hz), 7.41 (2H, brs), 8.12 (1H, d, J = 6.3 Hz), 8.39 (1H, brs), 8.47 (1H, d, J = 6.3 Hz), 9.60 (1H, d, J = 9.2 Hz), 10.05 (1H, brs).

IR (KBr) cm⁻¹: 3330, 1777, 1674, 1623, 1529, 1475, 1379, 1314, 1230, 1141, 1102, 1066, 1036.

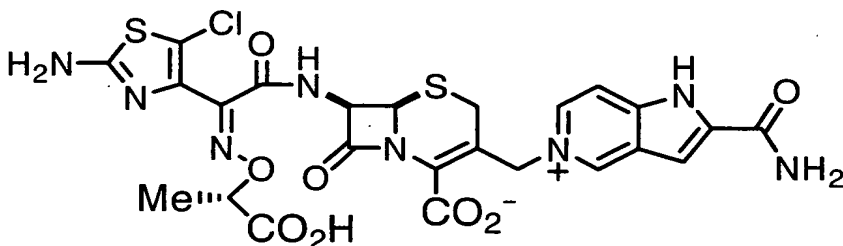
MS(ESI): 640⁺ (M+H)⁺.

Elementary Analysis as C₂₃H₂₂ClN₇O₉S₂ · 2.8H₂O.

Calculated : C,40.01; H,4.03; N,14.20; Cl,5.13; S,9.29 (%).

Found : C,39.92; H,3.90; N,14.32; Cl,5.27; S,9.31 (%).

Example 77



¹H-NMR (d₆-DMSO) δ : 1.35 (3H, d, J = 6.9 Hz), 3.05 and 3.48 (2H, ABq, J = 17.6 Hz), 4.53 (1H, q, J = 6.9 Hz), 5.06 (1H, d, J = 4.8 Hz), 5.13 (1H, d, J = 13.8 Hz), 5.64-5.73 (2H, m), 7.40 (2H, brs), 7.66 (1H, s), 7.87 (1H, brs), 7.94 (1H, d, J = 6.9 Hz), 8.51 (1H, brs), 8.97 (1H, d, J = 6.9 Hz), 9.62 (1H, brs), 9.81 (1H, brs).

IR (KBr) cm⁻¹: 3327, 3195, 1775, 1677, 1613, 1540, 1375, 1335, 1240, 1182, 1152, 1116, 1066, 1036.

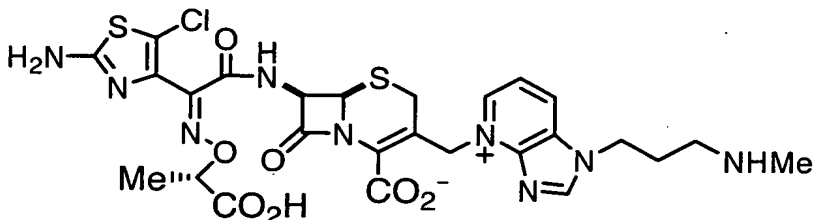
MS(ESI): 649⁺ (M+H)⁺.

Elementary Analysis as C₂₄H₂₁ClN₈O₈S₂ · 2.4H₂O.

Calculated : C,41.64; H,3.76; N,16.19; Cl,5.12; S,9.26 (%).

Found : C,41.70; H,3.71; N,16.24; Cl,5.00; S,9.063 (%).

Example 78



¹H-NMR (D₂O) δ : 1.43 (3H, d, J = 7.1 Hz), 2.39 (2H, quint. J = 7.8 Hz), 2.72 (3H, s), 3.15 (2H, t, J = 7.8 Hz), 3.26 and 3.62 (2H, ABq, J = 18.0 Hz), 4.59-4.69 (3H, m), 5.23 (1H, d, J = 4.8 Hz),
 5.62 (1H, d, J = 14.7 Hz), 5.70-5.75 (2H, m), 7.89 (1H, dd, J = 6.3, 8.3 Hz), 8.78 (1H, d, J = 8.3 Hz),
 8.86 (1H, brs), 8.88 (1H, d, J = 6.3 Hz).

IR (KBr) cm⁻¹: 3397, 2464, 1773, 1602, 1541, 1490, 1463, 1389, 1313, 1287, 1237, 1187, 1159, 1115, 1064, 1034.

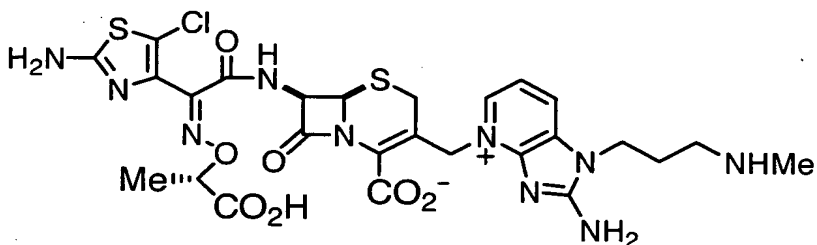
MS(ESI): 678⁺ (M+H)⁺.

10 Elementary Analysis as C₂₆H₂₈ClN₉O₇S₂ · 3.7H₂O.

Calculated : C,41.93; H,4.79; N,16.93; Cl,4.76; S,8.61 (%).

Found : C,41.93; H,4.74; N,16.89; Cl,4.53; S,8.58 (%).

Example 79



¹H-NMR (D₂O) δ : 1.44 (3H, d, J = 7.0 Hz), 2.20 (2H, m), 2.70 (3H, s), 3.12 (2H, m), 3.24 and 3.50 (2H, ABq, J = 17.9 Hz), 4.22 (2H, t, J = 7.1 Hz), 4.55 (1H, q, J = 7.0 Hz), 5.18 (1H, d, J = 4.8 Hz), 5.25 and 5.56 (2H, ABq, J = 14.7 Hz), 5.84 (1H, d, J = 4.8 Hz), 7.30 (1H, t-like), 7.89 (1H, d, J = 7.8 Hz), 8.12 (1H, d, J = 6.6 Hz).

20 IR (KBr) cm⁻¹: 3363, 3181, 1772, 1651, 1600, 1565, 1494, 1394, 1364, 1315, 1288, 1223, 1163, 1091, 1034.

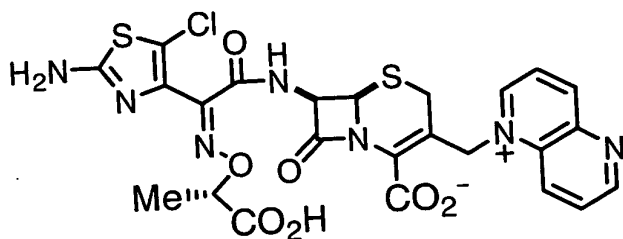
MS(ESI): 693⁺ (M+H)⁺.

Elementary Analysis as C₂₆H₂₉ClN₁₀O₇S₂ · 2.9H₂O.

Calculated : C,41.89; H,4.71; N,18.79; Cl,4.76; S,8.60 (%).

25 Found : C,41.93; H,4.73; N,18.81; Cl,4.51; S,8.51 (%).

Example 80



¹H-NMR (D₂O + DCl) δ : 1.55 (3H, d, J = 7.1 Hz), 3.35 and 3.63 (2H ABq, J = 18.9 Hz), 5.39 (1H, d, J = 5.1 Hz), 5.98 (1H, d, J = 5.1 Hz), 6.03 and 6.24 (2H, ABq, J = 15.6 Hz), 8.40 (1H, dd, J = 5.7, 8.7 Hz), 9.04 (1H, d, J = 9.3 Hz), 9.29 (1H, d, J = 8.7 Hz), 9.17-9.20 (2H, m).

5 IR (KBr) cm⁻¹: 3411, 3197, 1778, 1675, 1617, 1538, 1521, 1456, 1376, 1339, 1285, 1230, 1189, 1152, 1098, 1066, 1035.

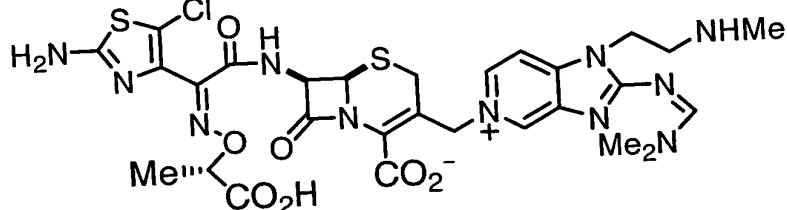
MS(ESD): 618⁺ (M+H)⁺.

Elementary Analysis as C₂₄H₂₀ClN₇O₇S₂ · 3.0H₂O.

Calculated : C,42.89; H,3.90; N,14.59; Cl,5.28; S,9.54 (%).

10 Found : C,42.91; H,3.97; N,12.66; Cl,5.18; S,9.51 (%).

Example 81



15 ¹H-NMR (D₂O + DCl) δ : 1.55 (3H, d, J = 7.2 Hz), 2.80 (3H, s), 3.38 and 3.77 (2H, ABq, J = 18.9 Hz), 3.38 (3H, s), 3.45 (3H, s), 3.64 (2H, t, J = 5.7 Hz), 4.76 (2H, t, J = 5.7 Hz), 4.99 (1H, q, J = 7.2 Hz), 5.37 (1H, d, J = 4.8 Hz), 5.42 and 5.88 (2H, ABq, J = 14.6 Hz), 5.95 (1H, d, J = 4.8 Hz), 8.13 (1H, d, J = 7.0 Hz), 8.68 (1H, brs), 8.84 (1H, dd, J = 1.2, 7.0 Hz), 9.14 (1H, d, J = 1.2 Hz).

IR (KBr) cm⁻¹: 3406, 1773, 1632, 1535, 1497, 1421, 1389, 1352, 1308, 1237, 1183, 1114, 1065, 1034.

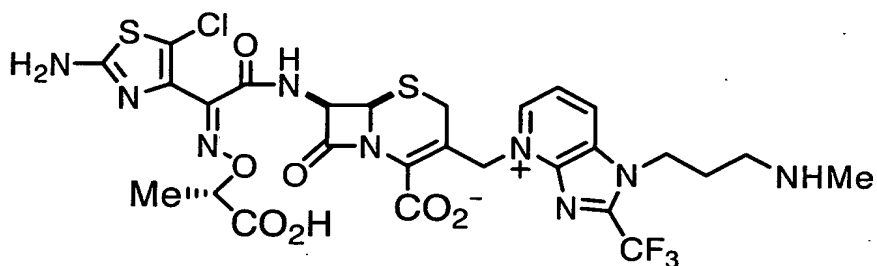
20 MS(FAB): 734⁺ (M+H)⁺.

Elementary Analysis as C₂₈H₃₂ClN₁₁O₇S₂ · 5.5H₂O.

Calculated : C,40.36; H,5.20; N,18.49; Cl,4.25; S,7.70 (%).

Found : C,40.38; H,5.03; N,18.36; Cl,4.52; S,7.89 (%).

25 Example 82



¹H-NMR (D₂O + DCl) δ : 1.44 (3H, d, J = 6.9 Hz), 2.39 (2H, m), 2.73 (3H, s), 3.23 (2H, m), 3.30 and 3.68 (2H, ABq, J = 18.0 Hz), 4.59-4.69 (3H, m), 5.24 (1H, d, J = 5.0 Hz), 5.67 and 5.93 (2H, ABq, J = 14.7 Hz), 5.88 (1H, d, J = 5.0 Hz), 8.09 (1H, dd, J = 8.2, 6.1 Hz), 8.99 (1H, d, J = 8.2 Hz), 9.12 (1H, d, J = 6.1 Hz).

IR (KBr) cm⁻¹: 3403, 2467, 1776, 1604, 1540, 1482, 1458, 1437, 1394, 1352, 1317, 1269, 1195, 1155, 1121, 1096, 1065, 1034.

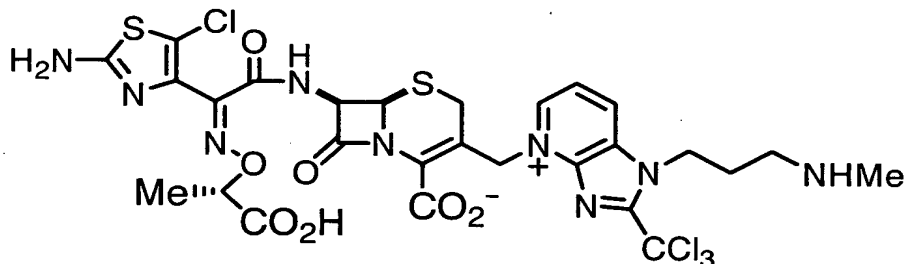
MS(FAB): 7462⁺ (M+H)⁺.

Elementary Analysis as C₂₇H₂₇ClF₃N₉O₇S₂ · 3.7H₂O.

Calculated : C,39.90; H,4.27; N,15.51; Cl,4.36; S,7.89 (%).

Found : C,39.98; H,4.33; N,15.51; Cl,4.12; S,7.73 (%).

Example 83



¹H-NMR (D₂O + DCl) δ : 1.56 (3H, d, J = 6.9 Hz), 2.50 (2H, m), 2.77 (3H, s), 3.33 (2H, m), 3.59 and 3.72 (2H, ABq, J = 18.3 Hz), 4.93-5.04 (3H, m), 5.27 (1H, d, J = 5.1 Hz), 5.77 and 6.28 (2H, ABq, J = 14.9 Hz), 5.92 (1H, d, J = 5.1 Hz), 8.05 (1H, dd, J = 8.4, 6.3 Hz), 8.99 (1H, d, J = 8.4 Hz), 9.03 (1H, d, J = 6.3 Hz).

IR (KBr) cm⁻¹: 3400, 1776, 1604, 1539, 1450, 1392, 1350, 1321, 1287, 1224, 1159, 1063, 1033.

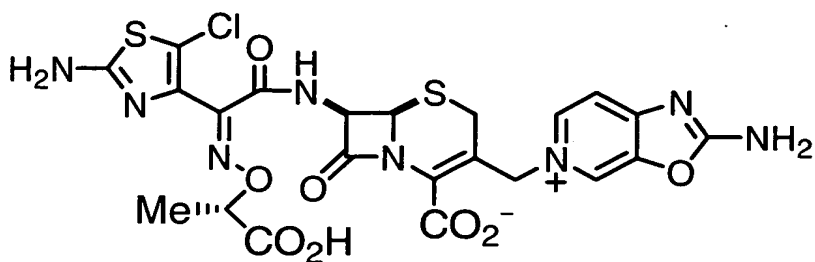
MS(FAB): 794⁺ (M+H)⁺.

Elementary Analysis as C₂₇H₂₇Cl₄N₉O₇S₂ · 3.3H₂O.

Calculated : C,37.93; H,3.96; N,14.74; Cl,16.59; S,7.50 (%).

Found : C,38.26; H,4.00; N,14.96; Cl,15.25; S,7.46 (%).

Example 84



¹H-NMR (d₆-DMSO) δ : 1.37 (3H, d, J = 7.1 Hz), 3.02 and 3.48 (2H, ABq, J = 17.9 Hz), 4.54 (1H, q, J = 7.1 Hz), 4.90 and 5.50 (2H, ABq, J = 13.5 Hz), 5.05 (1H, d, J = 4.8 Hz), 5.70 (1H, dd, J = 4.8, 8.7 Hz), 7.41 (2H, brs), 7.69 (1H, d, J = 6.8 Hz), 9.01 (1H, d, J = 6.8 Hz), 9.33 (2H, brs), 9.58 (2H, brs).

IR (KBr) cm⁻¹: 3393, 1776, 1687, 1615, 1559, 1513, 1484, 1377, 1326, 1284, 1213, 1188, 1154, 1106, 1066, 1034.

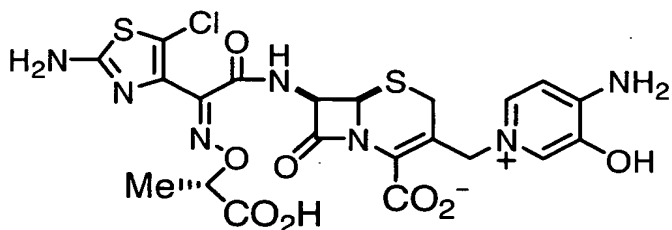
MS(FAB): 623⁺ (M+H)⁺.

10 Elementary Analysis as C₂₂H₁₉ClN₈O₈S₂ · 2.7H₂O.

Calculated : C,39.34; H,3.66; N,16.68; Cl,5.28; S,9.55 (%).

Found : C,39.35; H,3.67; N,16.61; Cl,5.26; S,9.48 (%).

Example 85



15

¹H-NMR (d₆-DMSO) δ : 1.39 (3H, d, J = 6.9 Hz), 2.95 and 3.42 (2H ABq, J = 17.4 Hz), 4.55 (1H, q, J = 6.9 Hz), 4.73 and 5.21 (2H, ABq, J = 13.8 Hz), 5.13 (1H, d, J = 4.8 Hz), 5.71 (1H, dd, J = 4.8, 8.7 Hz), 6.73 (1H, d, J = 6.9 Hz), 7.40 (2H, brs), 7.99 (1H, d, J = 6.9 Hz), 8.27 (1H, brs), 9.79 (1H, brs).

20 IR (KBr) cm⁻¹: 3343, 3202, 1776, 1644, 1546, 1446, 1370, 1309, 1258, 1179, 1147, 1065, 1036.

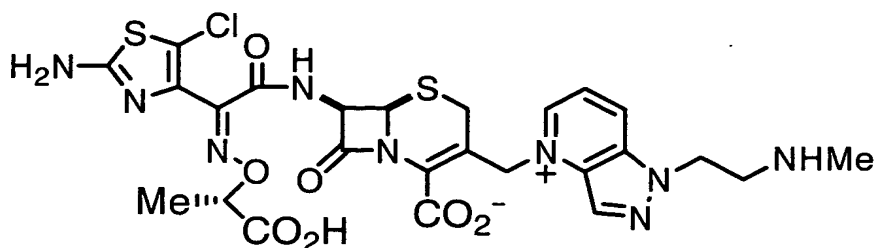
MS(FAB): 598⁺ (M+H)⁺.

Elementary Analysis as C₂₁H₂₀ClN₇O₇S₂ · 2.6H₂O.

Calculated : C,39.11; H,3.949; N,15.20; Cl,5.50; S,9.94 (%).

25 Found : C,39.18; H,3.74; N,15.14; Cl,5.38; S,9.82 (%).

Example 86



¹H-NMR (D₂O + DCl) δ : 1.44 (3H, d, J = 7.1 Hz), 2.80 (3H, s), 3.20 and 3.53 (2H, ABq, J = 17.9 Hz), 3.75 (2H, t, J = 5.5 Hz), 4.66 (1H, q, J = 7.1 Hz), 5.03 (2H, t, J = 5.5 Hz), 5.23 (1H, d, J = 5.0 Hz), 5.79 (2H, s), 5.88 (1H, d, J = 5.0 Hz), 8.07 (1H, dd, J = 8.7, 5.8 Hz), 8.82 (1H, s), 8.96 (1H, d, J = 8.7 Hz), 9.05 (1H, d, J = 5.8 Hz).

IR (KBr) cm⁻¹: 3408, 1773, 1604, 1540, 1476, 1447, 1394, 1352, 1316, 1289, 1222, 1187, 1159, 1080, 1034.

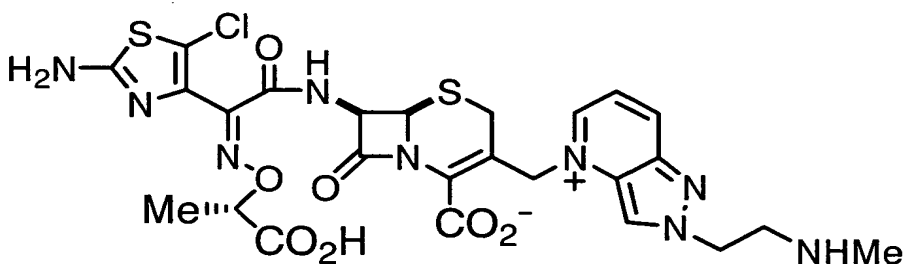
MS(FAB): 664⁺ (M+H)⁺.

10 Elementary Analysis as C₂₅H₂₆ClN₉O₇S₂ · 3.0H₂O.

Calculated : C,41.81; H,4.49; N,17.55; Cl,4.94; S,8.93 (%).

Found : C,41.86; H,4.45; N,17.66; Cl,4.81; S,8.71 (%).

Example 87



¹H-NMR (D₂O + DCl) δ : 1.44 (3H, d, J = 7.1 Hz), 2.78 (3H, s), 3.11 and 3.52 (2H, ABq, J = 17.9 Hz), 3.78 (2H, t, J = 5.6 Hz), 4.66 (1H, q, J = 7.1 Hz), 5.09 (2H, t, J = 5.6 Hz), 5.23 (1H, d, J = 4.8 Hz), 5.63 and 5.81 (2H, ABq, J = 15.2 Hz), 5.85 (1H, d, J = 4.8 Hz), 7.95 (1H, dd, J = 9.0, 5.4 Hz), 8.97 (1H, d, J = 9.0 Hz), 9.07 (1H, d, J = 5.4 Hz), 9.21 (1H, brs).

IR (KBr) cm⁻¹: 3408, 1773, 1603, 1540, 1476, 1447, 1394, 1352, 1316, 1289, 1223, 1187, 1159, 1080, 1034.

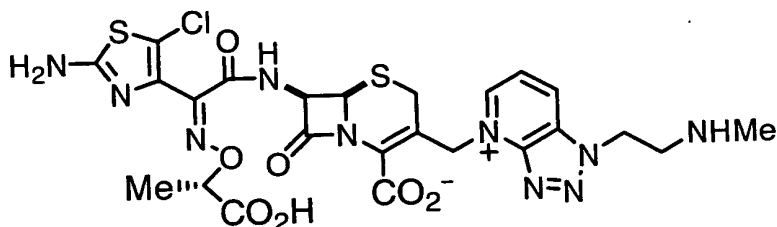
MS(FAB): 664⁺ (M+H)⁺.

Elementary Analysis as C₂₅H₂₆ClN₉O₇S₂ · 3.1H₂O.

Calculated : C,41.71; H,4.51; N,17.51; Cl,4.92; S,8.91 (%).

Found : C,41.75; H,4.39; N,17.57; Cl,4.64; S,8.71 (%).

Example 88



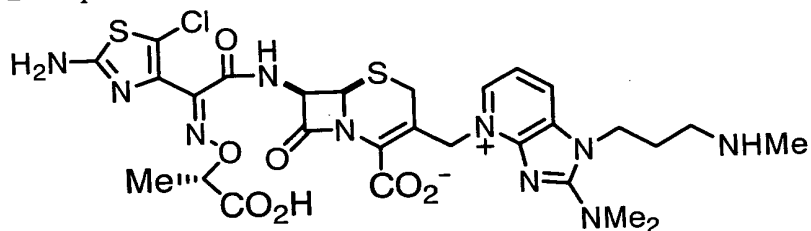
¹H-NMR (D₂O + DCl) δ : 1.55 (3H, d, J = 7.2 Hz), 2.85 (3H, s), 3.53 and 3.80 (2H, ABq, J = 18.0 Hz), 3.91 (2H, t, J = 6.0 Hz), 5.34 (1H, d, J = 4.8 Hz), 5.40 (2H, t, J = 6.0 Hz), 5.96 (1H, d, J = 4.8 Hz), 6.07 and 6.29 (2H, ABq, J = 15.0 Hz), 8.28 (1H, dd, J = 5.4, 8.4 Hz), 9.25 (1H, d, J = 8.4 Hz), 9.34 (1H, d, J = 5.4 Hz).

IR (KBr) cm⁻¹: 3408, 2448, 1774, 1606, 1539, 1465, 1393, 1348, 1283, 1188, 1155, 1093, 1065, 1034.

MS(ESI): 655 (M+H)⁺.

- 10 Elementary Analysis as C₂₄H₂₅ClN₁₀O₇S₂ · 3.6H₂O.
 Calculated : C,39.49; H,4.45; N,19.19; Cl,4.86; S,8.79 (%).
 Found : C,39.50; H,4.42; N,19.21; Cl,4.80; S,8.67 (%).

Example 89



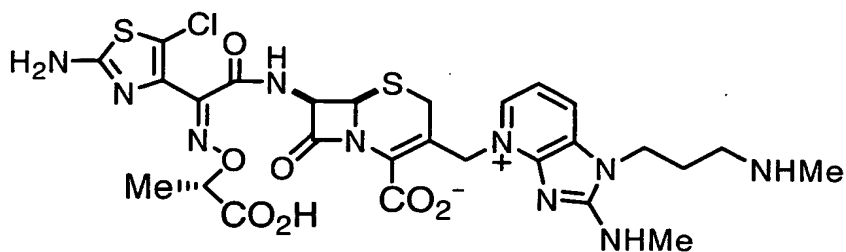
- 15 ¹H-NMR (D₂O) δ : 1.44 (3H, d, J = 7.0 Hz), 2.22 (2H, m), 2.70 (3H, s), 3.08 (2H, m), 3.27 and 3.51 (2H, ABq, J = 18.0 Hz), 3.36 (6H, s), 4.36 (2H, t-like), 5.16 (1H, d, J = 4.5 Hz), 5.22 and 5.67 (2H, ABq, J = 14.7 Hz), 5.83 (1H, d, J = 4.5 Hz), 7.26 (1H, t-like), 7.85 (1H, d, J = 7.8 Hz), 8.08 (1H, d, J = 6.6 Hz).

- 20 IR (KBr) cm⁻¹: 3399, 1773, 1629, 1584, 1541, 1501, 1419, 1350, 1320, 1226, 1167, 1137, 1064, 1033.

MS(FAB): 721⁺ (M+H)⁺.

- Elementary Analysis as C₂₈H₃₃ClN₁₀O₇S₂ · 3.0H₂O.
 Calculated : C,43.38; H,5.07; N,18.07; Cl,4.57; S,8.27 (%).
 25 Found : C,43.43; H,5.05; N,18.07; Cl,4.36; S,8.10 (%).

Example 90



¹H-NMR (D₂O+DCI) δ : 1.56 (3H, d, J = 7.5 Hz), 2.22 (2H, m), 2.72 (3H, s), 3.12-3.18 (5H, m), 3.46 and 3.60 (2H, ABq, J = 18.5 Hz), 4.22 (2H, t, J = 7.5 Hz), 5.01 (1H, q, J = 7.5 Hz), 5.27 (1H, d, J = 4.8 Hz), 5.27 (1H, d, J = 4.8 Hz), 5.43 (1H, d, J = 15.0 Hz), 5.85-5.91 (2H, m), 7.32 (1H, dd, J = 6.7, 7.6 Hz), 7.92 (1H, d, J = 7.6 Hz), 8.10 (1H, d, J = 6.7 Hz).

IR (KBr) cm⁻¹: 3398, 1773, 1642, 1596, 1541, 1496, 1412, 1392, 1366, 1316, 1222, 1165, 1139, 1099, 1064, 1034.

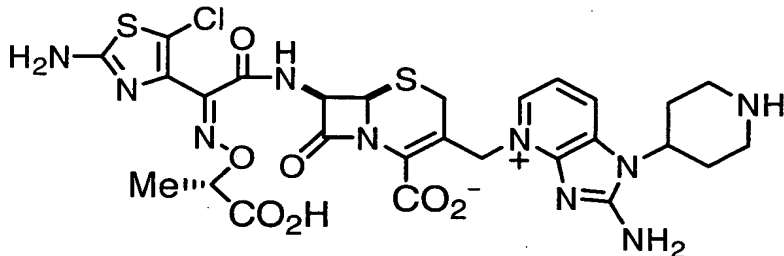
MS(ESI): 707⁺ (M+H)⁺.

Elementary Analysis as C₂₇H₃₁ClN₁₀O₇S₂ · 3.5H₂O.

Calculated : C,42.10; H,4.97; N,18.18; Cl,4.60; S,8.33 (%).

Found : C,42.09; H,4.97; N,18.19; Cl,4.44; S,8.18 (%).

Example 91



¹H-NMR (D₂O+DCI) δ : 1.55 (3H, d, J = 7.2 Hz), 2.33 (2H, d-like), 2.61 (2H, q-like), 3.25-3.39 (3H, m), 3.60 (1H, d, J = 18.3 Hz), 3.72 (2H, d-like), 4.99 (1H, q, J = 7.2 Hz), 5.29 (1H, d, J = 4.9 Hz), 5.50 and 5.69 (2H, ABq, J = 15.0 Hz), 5.92 (1H, d, J = 4.9 Hz), 7.33 (1H, t-like), 8.14 (2H, m).
IR (KBr) cm⁻¹: 3380, 3182, 1772, 1601, 1555, 1491, 1440, 1395, 1362, 1317, 1287, 1225, 1169, 1092, 1033.

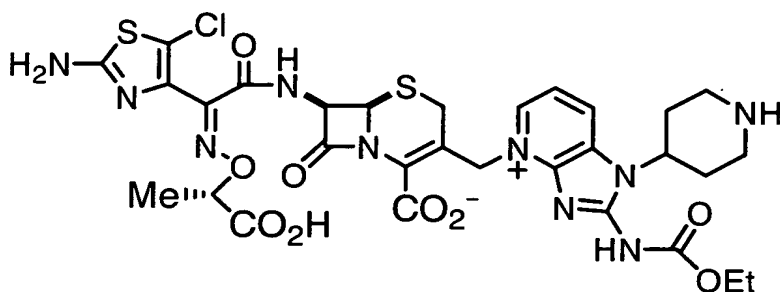
MS(ESI): 705⁺ (M+H)⁺.

Elementary Analysis as C₂₇H₂₉ClN₁₀O₇S₂ · 4.5H₂O.

Calculated : C,41.25; H,4.87; N,17.81; Cl,4.51; S,8.16 (%).

Found : C,41.38; H,4.79; N,17.71; Cl,4.19; S,7.50 (%).

Example 92



¹H-NMR (D₂O + DCl) δ : 1.36 (3H, d, J = 7.1 Hz), 1.55 (3H, t, J = 7.3 Hz), 2.38 (2H, d-like), 2.62-2.72 (2H, m), 3.27-3.35 (2H, m), 3.44 (1H, d, J = 18.6 Hz), 3.68-3.74 (3H, m), 4.37 (2H, q, J = 7.3 Hz), 4.99 (1H, q, J = 7.1 Hz), 5.31 (1H, d, J = 5.1 Hz), 5.73 (1H, d, J = 15.1 Hz), 5.90-5.95 (2H, m), 7.74 (1H, dd, J = 6.6, 7.9 Hz), 8.63 (1H, d, J = 6.6 Hz), 8.69 (1H, d, J = 7.9 Hz).

IR (KBr) cm⁻¹: 3409, 2982, 2527, 1775, 1607, 1538, 1468, 1385, 1283, 1223, 1174, 1094, 1033.

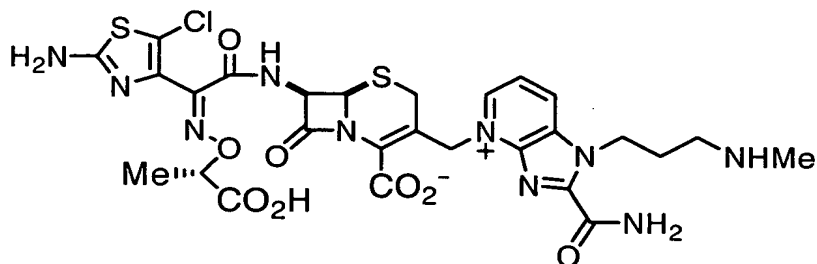
MS(ESI): 777⁺ (M+H)⁺.

Elementary Analysis as C₃₀H₃₃ClN₁₀O₉S₂ · 4.8H₂O.

Calculated : C, 41.72; H, 4.97; N, 16.22; Cl, 4.10; S, 7.43 (%).

Found : C, 41.68; H, 4.86; N, 16.33; Cl, 4.08; S, 7.46 (%).

Example 93



¹H-NMR (D₂O+DCl) δ : 1.56 (3H, d, J = 5.4 Hz), 2.38 (2H, m), 2.74 (3H, s), 3.19 (2H, m), 3.54 (2H, m), 4.96 (3H, m), 5.19 (1H, brs), 5.62-6.32 (2H, m), 5.87 (1H, brs), 7.99 (1H, m), 8.93 (1H, d, J = 7.5 Hz), 9.01 (1H, d, J = 5.7 Hz).

IR (KBr) cm⁻¹: 3399, 1771, 1698, 1667, 1602, 1540, 1460, 1394, 1358, 1327, 1287, 1221, 1187, 1152, 1082, 1061, 1034.

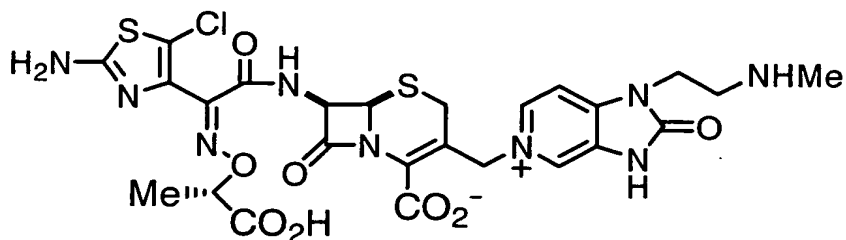
MS(ESI): 721⁺ (M+H)⁺.

Elementary Analysis as C₂₇H₂₉ClN₁₀O₈S₂ · 5.0 H₂O.

Calculated : C, 39.97; H, 4.85; N, 17.27; Cl, 4.37; S, 7.91 (%).

Found : C, 39.88; H, 4.45; N, 17.07; Cl, 4.40; S, 7.99 (%).

Example 94



$^1\text{H-NMR}$ ($\text{D}_2\text{O} + \text{DCl}$) δ : 1.55 (3H, d, $J = 7.1$ Hz), 2.79 (3H, s), 3.35 and 3.54 (2H, ABq, $J = 18.5$ Hz), 3.54 (2H, t, $J = 5.6$ Hz), 4.44 (2H, t, $J = 5.6$ Hz), 4.99 (1H, q, $J = 7.1$ Hz), 5.36 (1H, d, $J = 5.0$ Hz), 5.31 and 5.79 (2H, ABq, $J = 14.7$ Hz), 5.94 (1H, d, $J = 5.0$ Hz), 7.79 (1H, d, $J = 6.7$ Hz), 8.65 (1H, dd, $J = 1.2, 6.7$ Hz), 8.72 (1H, brs).

IR (KBr) cm^{-1} : 3395, 3086, 1748, 1660, 1611, 1528, 1448, 1396, 1353, 1313, 1288, 1212, 1188, 1156, 1136, 1111, 1106, 1035.

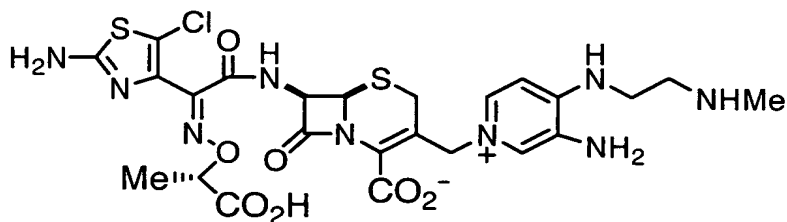
MS(ESI): $680^+ (\text{M}+\text{H})^+$.

Elementary Analysis as $\text{C}_{25}\text{H}_{26}\text{ClN}_9\text{O}_8\text{S}_2 \cdot 3.4\text{H}_2\text{O}$.

Calculated: C, 40.50; H, 4.46; N, 17.00; Cl, 4.78; S, 8.56 (%).

Found: C, 40.73; H, 4.45; N, 17.10; Cl, 4.65; S, 8.35 (%).

Example 95



$^1\text{H-NMR}$ ($\text{D}_2\text{O} + \text{DCl}$) δ : 1.56 (3H, d, $J = 7.1$ Hz), 2.79 (3H, s), 3.31 and 3.66 (2H, ABq, $J = 18.3$ Hz), 3.40 (2H, t, $J = 5.9$ Hz), 3.85 (2H, t, $J = 5.9$ Hz), 4.96-5.03 (2H, m), 5.33 (1H, d, $J = 5.1$ Hz), 5.41 (1H, d, $J = 14.7$ Hz), 5.93 (1H, d, $J = 5.1$ Hz), 6.95 (1H, d, $J = 7.2$ Hz), 7.71 (1H, d, $J = 1.8$ Hz), 8.05 (1H, dd, $J = 1.8, 7.2$ Hz).

IR (KBr) cm^{-1} : 3368, 1773, 1627, 1556, 1455, 1395, 1349, 1321, 1287, 1190, 1158, 1093, 1065, 1034.

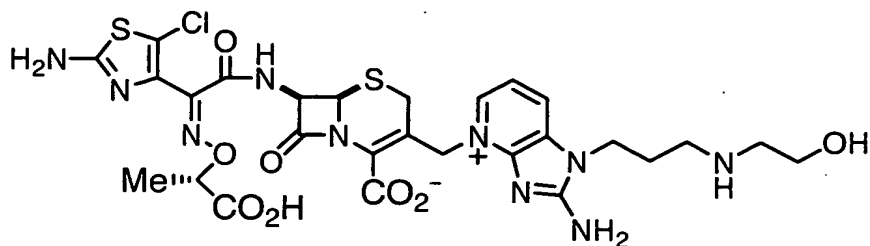
MS(ESI): $654^+ (\text{M}+\text{H})^+$.

Elementary Analysis as $\text{C}_{24}\text{H}_{28}\text{ClN}_9\text{O}_7\text{S}_2 \cdot 3.1\text{H}_2\text{O}$.

Calculated: C, 40.60; H, 4.86; N, 17.76; Cl, 4.993; S, 9.03 (%).

Found: C, 40.63; H, 4.81; N, 17.74; Cl, 4.891; S, 8.88 (%).

Example 96



¹H-NMR (D₂O + DCl) δ : 1.55 (3H, d, J = 7.0 Hz), 2.21-2.32 (2H, m), 3.20-3.25 (4H, m), 3.37 and 3.61 (2H, ABq, J = 18.5 Hz), 3.83 (2H, t, J = 5.0 Hz), 4.29 (2H, t, J = 7.1 Hz), 4.99 (1H, q, J = 7.0 Hz), 5.29 (1H, d, J = 4.5 Hz), 5.50 and 5.68 (2H, ABq, J = 15.2 Hz), 5.92 (1H, d, J = 4.5 Hz), 7.34 (2H, t-like), 7.66 (1H, d, J = 7.8 Hz), 8.13 (1H, d, J = 6.6 Hz).

IR (KBr) cm⁻¹: 3368, 1773, 1627, 1556, 1455, 1395, 1349, 1321, 1287, 1090, 1158, 1093, 1065, 1034.

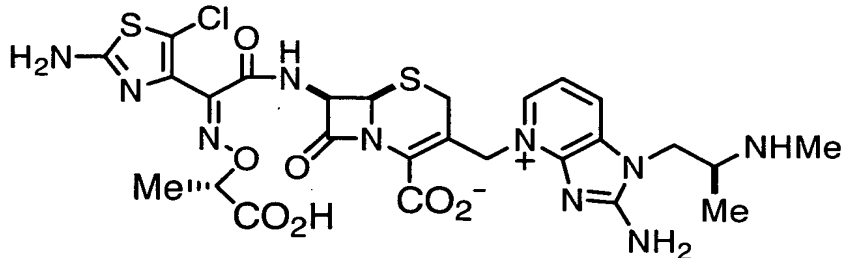
MS(ESI): 723⁺ (M+H)⁺.

Elementary Analysis as C₂₇H₃₁ClN₁₀O₈S₂ · 2.8H₂O.

Calculated : C,41.92; H,4.77; N,18.11; Cl,4.58; S,8.29 (%).

Found : C,41.93; H,4.73; N,18.06; Cl,4.46; S,8.17 (%).

Example 97



¹H-NMR (D₂O + DCl) δ : 1.43 (3H, d, J = 6.9 Hz), 1.55 (3H, d, J = 7.2 Hz), 2.78 (3H, s), 3.40 and 3.61 (2H, ABq, J = 18.6 Hz), 3.83-3.95 (1H, m), 4.39-4.60 (2H, m), 5.00 (1H, q, J = 6.9 Hz), 5.29 (1H, d, J = 4.8 Hz), 5.51 and 5.72 (2H, ABq, J = 15.2 Hz), 5.92 (1H, d, J = 4.8 Hz), 7.34 (1H, dd, J = 6.9, 8.1 Hz), 8.02 (1H, d, J = 8.1 Hz), 8.18 (1H, d, J = 6.9 Hz).

IR (KBr) cm⁻¹: 3372, 3185, 1772, 1667, 1600, 1563, 1493, 1394, 1353, 1317, 1287, 1225, 1166, 1090, 1033.

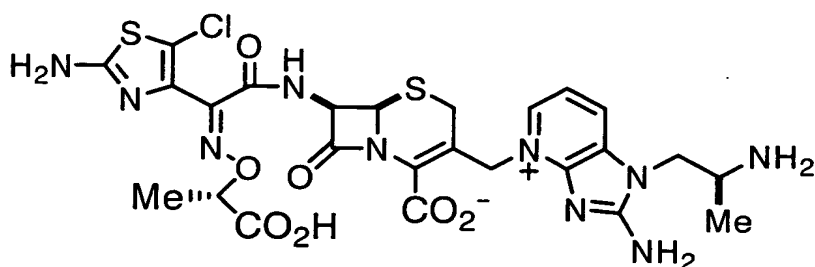
MS(ESI): 693 (M+H)⁺.

Elementary Analysis as C₂₆H₂₉ClN₁₀O₇S₂ · 2.7H₂O.

Calculated : C,42.10; H,4.67; N,18.88; Cl,4.78; S,8.65 (%).

Found : C,42.15; H,4.72; N,18.88; Cl,4.61; S,8.40 (%).

Example 98



¹H-NMR (D₂O+DCI) δ : 1.44 (3H, d, J = 6.3 Hz), 1.55 (3H, d, J = 7.2 Hz), 3.38 and 3.59 (2H, ABq, J = 18.6 Hz), 3.96 (1H, m), 4.41 (2H, d, J = 5.7 Hz), 4.98 (1H, q, J = 7.2), 5.27 (1H, d, J = 4.7 Hz), 5.47 and 5.71 (2H, ABq, J = 14.6 Hz), 5.91 (1H, d, J = 4.7 Hz), 7.35 (1H, m), 8.00 (1H, d, J = 8.1 Hz), 8.17 (1H, d, J = 6.9 Hz).

IR (KBr) cm⁻¹: 3358, 3184, 1771, 1651, 1563, 1494, 1396, 1365, 1317, 1288, 1225, 1166, 1090, 1034.

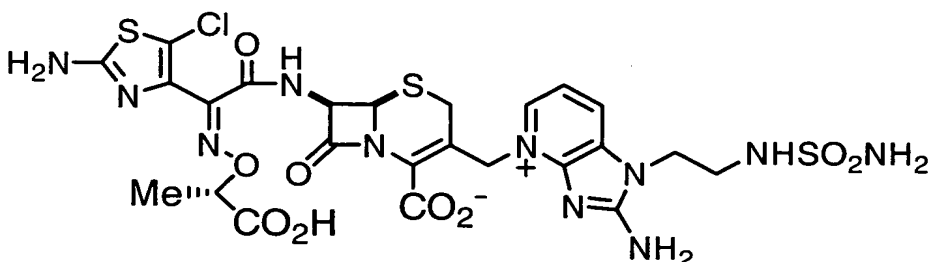
MS(ESI): 679⁺(M+H⁺).

Elementary Analysis as C₂₅H₂₇ClN₁₀O₇S₂ · 2.9 H₂O.

Calculated : C,41.06 ; H,4.52 ; N,19.15 ; Cl,4.85; S,8.77 (%).

Found : C,41.06 ; H,4.46 ; N,19.14 ; Cl,4.75; S,8.62 (%).

Example 99



¹H-NMR (d₆-DMSO) δ : 1.36 (3H, d, J = 7.0 Hz), 2.96 and 3.47 (2H, ABq, J = 17.7 Hz), 3.26 (2H, brs), 4.21 (2H, brs), 4.53 (1H, q, J = 7.0 Hz), 5.03 (1H, q, J = 5.1 Hz), 5.26 and 5.38 (2H, ABq, J = 13.5 Hz), 5.72 (1H, dd, J = 5.1, 9.0 Hz), 6.67 (2H, brs), 6.83 (1H, brs), 7.30 (1H, t-like), 7.41 (2H, brs), 7.93 (1H d, J = 7.5 Hz), 8.51 (1H, brs), 8.81 (1H, d, J = 6.6 Hz), 9.80 (1H, brs).

IR (KBr) cm⁻¹: 3382, 3194, 1766, 1667, 1651, 1609, 1568, 1496, 1444, 1389, 1345, 1304,

1214, 1156, 1076, 1036.

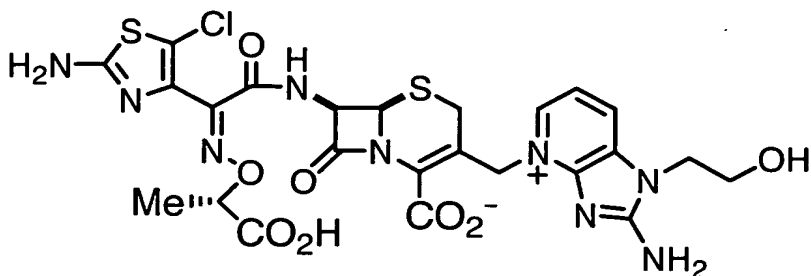
MS(ESI): 744⁺(M+H⁺).

Elementary Analysis as C₂₄H₂₆ClN₁₁O₉S₃ · 3.0H₂O.

Calculated : C,36.11; H,4.04; N,19.30; Cl,4.44; S,12.05 (%).

Found : C,35.88; H,3.93; N,19.18; Cl,4.54; S,12.17 (%).

Example 100



¹H-NMR (D₂O + DCl) δ : 1.54 (3H, d, J = 6.9 Hz), 3.36 and 3.61 (2H, ABq, J = 18.6 Hz), 3.97 (2H, t, J = 4.8 Hz), 4.30 (2H, t, J = 4.8 Hz), 5.29 (1H, d, J = 4.8 Hz), 5.54 and 5.68 (2H, ABq, J = 15.3 Hz), 5.92 (1H, d, J = 4.8 Hz), 7.34 (1H, t-like), 7.97 (1H d, J = 7.8 Hz), 8.14 (1H, d, J = 6.9 Hz).

IR (KBr) cm⁻¹: 3357, 3190, 1758, 1669, 1648, 1618, 1574, 1540, 1492, 1460, 1443, 1412, 1395, 1362, 1342, 1297, 1265, 1236, 1210, 1168, 1074, 1028.

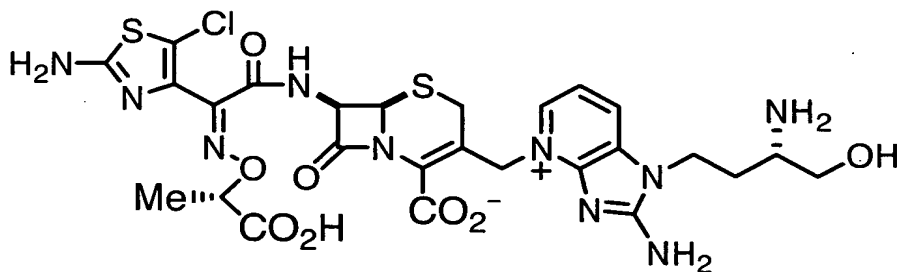
MS(ESI): 666⁺ (M+H)⁺.

10 Elementary Analysis as C₂₄H₂₄ClN₉O₈S₂ · 1.7H₂O.

Calculated : C,41.37; H,3.96; N,18.09; Cl,5.09; S,9.20 (%).

Found : C,41.53; H,3.80; N,18.19; Cl,4.64; S,8.79 (%).

Example 101



15

¹H-NMR (D₂O + DCl) δ : 1.55 (3H, d, J = 7.1Hz), 2.20 (2H, m), 3.37 (1H, d, J = 18.3 Hz), 3.50-3.64 (2H, m), 3.77 (1H, dd, J = 6.0, 12.3 Hz), 3.94 (1H, dd, J = 4.2, 12.3 Hz), 4.30 (2H, t, J = 7.8 Hz), 5.30 (1H, d, J = 4.8 Hz), 5.51 and 5.68 (2H, ABq, J = 15.2 Hz), 5.92 (1H, d, J = 4.8 Hz), 7.35 (1H, t-like), 8.00 (1H d, J = 7.8 Hz), 8.14 (1H, d, J = 6.6 Hz).

20 IR (KBr) cm⁻¹: 3613, 3415, 3339, 3191, 1763, 1703, 1670, 1620, 1570, 1532, 1497, 1443, 1392, 1357, 1345, 1309, 1289, 1265, 1214, 1168, 1154, 1084, 1061, 1029.

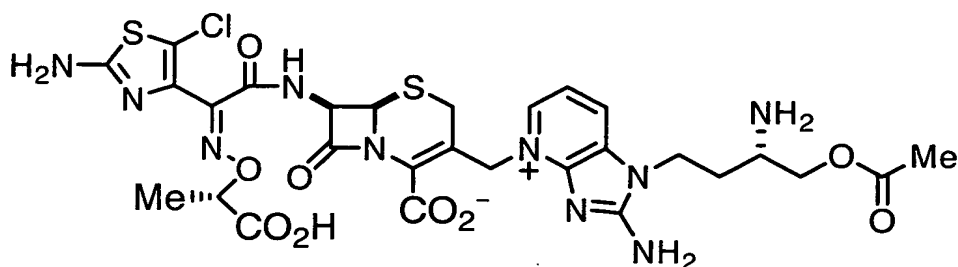
MS(ESI): 709⁺ (M+H)⁺.

Elementary Analysis as C₂₆H₂₉ClN₁₀O₈S₂ · 2.3H₂O.

Calculated : C,41.60; H,4.51; N,18.66; Cl,4.72; S,8.54 (%).

25 Found : C,41.66; H,4.19; N,18.68; Cl,4.65; S,7.87 (%).

Example 102



¹H-NMR (D₂O + DCl) δ : 1.55 (3H, d, J = 7.2 Hz), 2.13 (3H, s), 2.17-2.35 (2H, m), 3.38 and 3.61
 5 (2H, ABq, J = 18.6 Hz), 3.74-3.81 (1H, m), 4.24-4.44 (4H, m), 4.99 (1H, q, J = 7.2 Hz), 5.29 (1H, d, J = 4.8 Hz), 5.51 and 5.69 (2H, ABq, J = 15.0 Hz), 5.92 (1H, d, J = 4.8 Hz), 7.36 (1H, dd, J = 6.6, 8.1 Hz), 8.00 (1H d, J = 8.1 Hz), 8.15 (1H, d, J = 6.6 Hz).

IR (KBr) cm⁻¹: 3371, 3182, 1773, 1651, 1604, 1562, 1495, 1393, 1367, 1317, 1285, 1229, 1166, 1035.

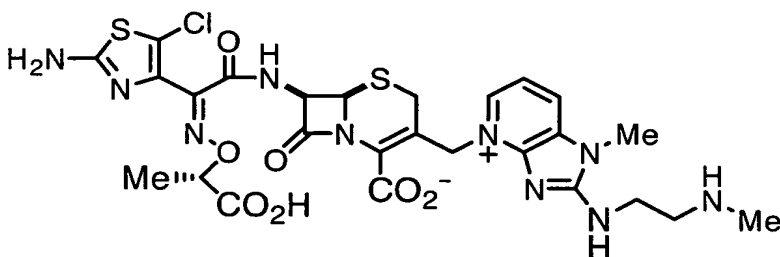
10 MS(ESI): 751⁺ (M+H)⁺.

Elementary Analysis as C₂₈H₃₁ClN₁₀O₉S₂ · 3.4H₂O.

Calculated : C,41.39; H,4.69; N,17.24; Cl,4.36; S,7.89 (%).

Found : C,41.23; H,4.31; N,17.10; Cl,4.01; S,7.97 (%).

15 Example 103



¹H-NMR (D₂O+DCl) δ : 1.55 (3H, d, J = 7.5 Hz), 3.37-3.57 (4H, m), 3.67 (3H, s), 3.93-4.02 (2H, m), 5.00 (1H, sept, J = 7.5 Hz), 5.25 (1H, d, J = 5.1 Hz), 5.46 and 5.93 (2H, ABq, J = 15.0 Hz), 5.91 (1H, d, J = 5.1), 7.53 (1H, t, J = 6.6 Hz), 7.94 (1H, d, J = 6.6 Hz), 8.15 (1H, d, J = 6.6 Hz).

20 IR (KBr) cm⁻¹: 3309, 1773, 1636, 1598, 1539, 1501, 1452, 1390, 1357, 1317, 1285, 1142, 1093, 1072, 1034, 988.

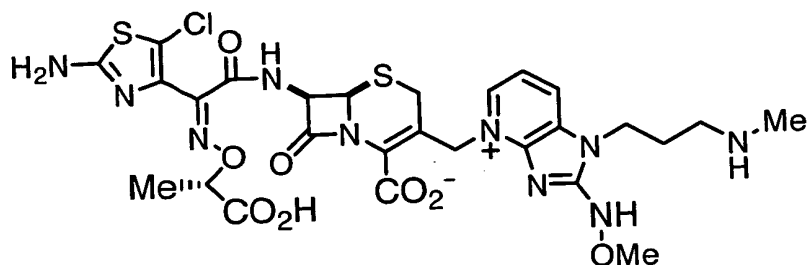
MS(ESI): 693⁺ (M+H)⁺.

Elementary Analysis as C₂₆H₂₉ClN₁₀O₇S₂ · 3.9 H₂O.

Calculated : C,41.89 ; H,4.71 ; N,18.79 ; Cl,4.76; S,8.60 (%).

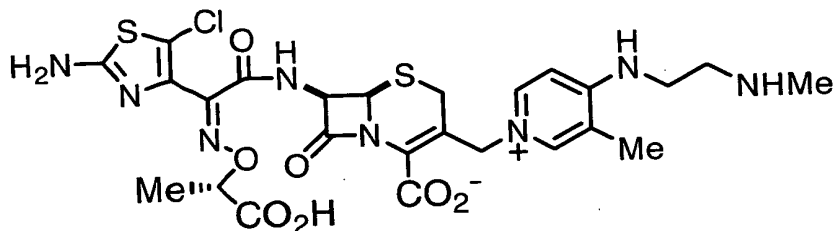
25 Found : C,42.03 ; H,4.98 ; N,18.70 ; Cl,4.60; S,8.57 (%).

Example 104



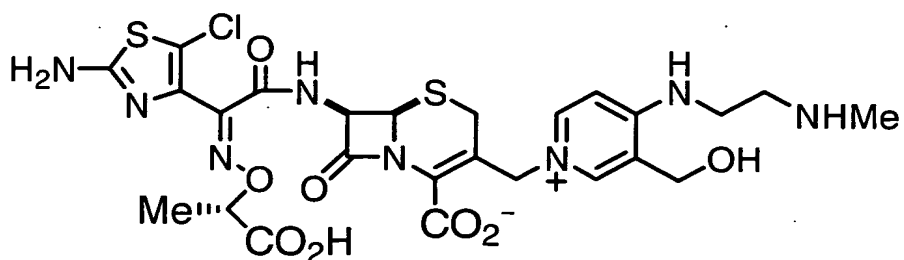
- ¹H-NMR (D₂O+DCI) δ : 1.54 (3H, d, J = 7.2 Hz), 2.17-2.30 (2H, m), 2.72 (3H, s), 3.11-3.20 (2H, m), 3.36 and 3.66 (2H, ABq, J = 18.3 Hz), 3.94 (3H, s), 4.18-4.27 (2H, m), 4.97 (1H, sept, J = 7.2 Hz), 5.30 (1H, d, J = 5.1 Hz), 5.60 and 5.73 (2H, ABq, J = 15.2 Hz), 5.92 (1H, d, J = 5.1 Hz), 7.44-7.50 (1H, m), 8.14 (1H, d, J = 8.1 Hz), 8.28 (1H, d, J = 6.3 Hz).
 IR (KBr) cm⁻¹: 3398, 1775, 1599, 1490, 1393, 1315, 1223, 1162, 1095, 1063, 1035, 968.
 MS(ESI): 723⁺ (M+H)⁺.
 10 Elementary Analysis as C₂₇H₃₁ClN₁₀O₈S₂ · 3.7 H₂O.
 Calculated : C, 41.06 ; H, 4.90 ; N, 17.73 ; Cl, 4.49 ; S, 8.12 (%).
 Found : C, 41.11 ; H, 4.67 ; N, 17.59 ; Cl, 4.59 ; S, 8.01 (%).

Example 105



- ¹H-NMR (D₂O + DCI) δ : 1.45 (3H, d, J = 6.9 Hz), 2.18 (3H, s), 2.76 (3H, s), 3.15 and 3.55 (2H, ABq, J = 18.0 Hz), 3.34 (2H, t, J = 6.0 Hz), 3.80 (2H, t, J = 6.0 Hz), 4.68 (1H, q, J = 6.9 Hz), 4.89 and 5.09 (2H, ABq, J = 14.7 Hz), 5.23 (1H, d, J = 4.8 Hz), 5.85 (1H, d, J = 4.8 Hz), 6.93 (1H, d, J = 7.2 Hz), 8.08 (1H, brs), 8.22 (1H, d, J = 7.2 Hz).
 20 IR (KBr) cm⁻¹: 3383, 1773, 1649, 1554, 1449, 1395, 1288, 1213, 1190, 1154, 1094, 1065, 1035.
 MS(ESI): 653⁺ (M+H)⁺.
 Elementary Analysis as C₂₅H₂₉ClN₈O₇S₂ · 3.0 H₂O.
 Calculated : C, 42.46 ; H, 4.99 ; N, 15.85 ; Cl, 5.01 ; S, 9.07 (%).
 25 Found : C, 42.47 ; H, 4.77 ; N, 15.81 ; Cl, 5.86 ; S, 8.84 (%).

Example 106



¹H-NMR (D₂O + DCl) δ : 1.45 (3H, d, J = 7.2 Hz), 2.76 (3H, s), 3.16 and 3.58 (2H, ABq, J = 17.4 Hz), 3.36 (2H, t, J = 6.3 Hz), 3.82 (2H, t, J = 6.3 Hz), 4.64-4.72 (3H, m), 4.91 and 5.13 (2H, ABq, J = 14.7 Hz), 5.24 (1H, d, J = 4.8 Hz), 5.86 (1H, d, J = 4.8 Hz), 7.02 (1H, d, J = 7.5 Hz), 8.24 (1H, brs), 8.29 (1H, d, J = 7.5 Hz).

IR (KBr) cm⁻¹: 3366, 1772, 1651, 1588, 1551, 1457, 1395, 1288, 1205, 1150, 1094, 1035.

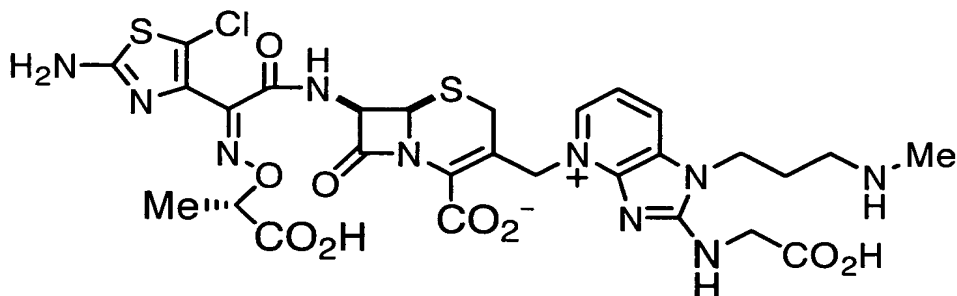
MS(ESI): 669⁺ (M+H)⁺.

Elementary Analysis as C₂₅H₂₉ClN₈O₈S₂ · 3.3H₂O.

Calculated : C,41.21; H,4.93; N,15.38; Cl,4.87; S,8.80 (%).

Found : C,41.38; H,4.73; N,15.53; Cl,4.77; S,8.51 (%).

Example 107



¹H-NMR (D₂O+DCl) δ : 1.56 (3H, d, J = 6.9 Hz), 2.18-2.31 (2H, m), 2.71 (3H, s), 3.11-3.19 (2H, m), 3.43 and 3.51 (2H, ABq, J = 17.9 Hz), 4.25-4.35 (2H, m), 4.43 (2H, s), 4.18 (1H, sept, J = 6.9 Hz), 5.20 (1H, d, J = 4.8 Hz), 5.35 and 5.91 (2H, ABq, J = 15.2 Hz), 5.90 (1H, d, J = 4.8 Hz), 7.34-7.40 (1H, m), 8.02 (1H, d, J = 7.5 Hz), 8.18 (1H, d, J = 6.6 Hz).

IR (KBr) cm⁻¹: 3409, 1774, 1635, 1593, 1540, 1496, 1390, 1314, 1228, 1188, 1165, 1112, 1073, 1034, 984, 759.

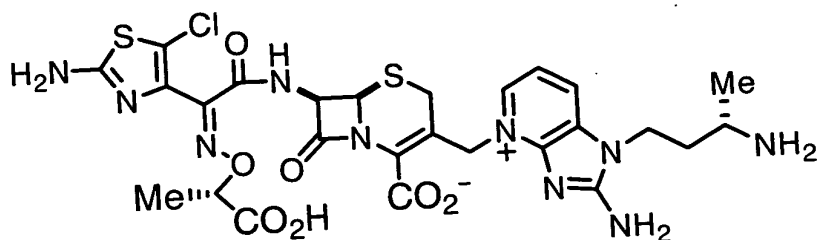
MS(FAB): 751⁺ (M+H)⁺.

Elementary Analysis as C₂₈H₃₁ClN₁₀O₉S₂ · 2.3 H₂O.

Calculated : C,42.43 ; H,4.53 ; N,17.67 ; Cl,4.47; S,8.09 (%).

Found : C,42.50 ; H,4.16 ; N,17.66 ; Cl,4.40; S,7.88 (%).

Example 108



¹H-NMR (D₂O+DCI) δ : 1.43 (3H, d, J = 6.9 Hz), 1.55 (3H, d, J = 7.1 Hz), 2.17 (2H, m), 3.35 and 3.59 (2H, ABq, J = 18.6 Hz), 3.51 (1H, m), 4.28 (2H, t-like), 4.97 (1H, q, J = 7.1), 5.27 (1H, d, J = 4.8 Hz), 5.45 and 5.67 (2H, ABq, J = 15.0 Hz), 5.91 (1H, d, J = 4.8 Hz), 7.3 (1H, t-like), 7.97 (1H, d, J = 7.8 Hz), 8.13 (1H, d, J = 6.9 Hz).

IR (KBr) cm⁻¹: 3408, 1773, 1650, 1601, 1565, 1495, 1395, 1363, 1317, 1287, 1224, 1165, 1090, 1034.

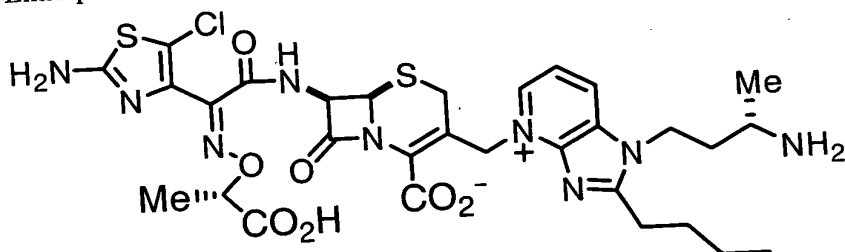
MS(ESI): 693⁺(M+H⁺).

10 Elementary Analysis as C₂₆H₂₉ClN₁₀O₇S₂ · 3.7 H₂O.

Calculated : C, 41.10 ; H, 4.83 ; N, 18.43 ; Cl, 4.67 ; S, 8.44 (%).

Found : C, 41.15 ; H, 4.69 ; N, 18.33 ; Cl, 4.65 ; S, 8.17 (%).

Example 109



15 ¹H-NMR (D₂O+DCI) δ : 0.97 (3H, t, J = 7.4 Hz), 1.48 (2H, m), 1.55 (3H, d, J = 7.2 Hz), 1.91 (2H, q, J = 7.5 Hz), 2.23 (2H, m), 3.15 (2H, t, J = 7.5 Hz), 3.42 and 3.64 (2H, ABq, J = 18.3 Hz), 3.61 (1H, m), 4.58 (2H, t-like), 4.99 (1H, q, J = 7.2), 5.28 (1H, d, J = 4.8 Hz), 5.73 and 6.02 (2H, ABq, J = 15.0 Hz), 5.73 (1H, d, J = 4.8 Hz), 7.79 (1H, t-like), 8.67 (1H, d, J = 8.1 Hz), 8.72 (1H, d, J = 6.3

20 Hz).

IR (KBr) cm⁻¹: 3399, 2959, 2872, 1776, 1601, 1540, 1465, 1396, 1349, 1318, 1224, 1161, 1093, 1064, 1033.

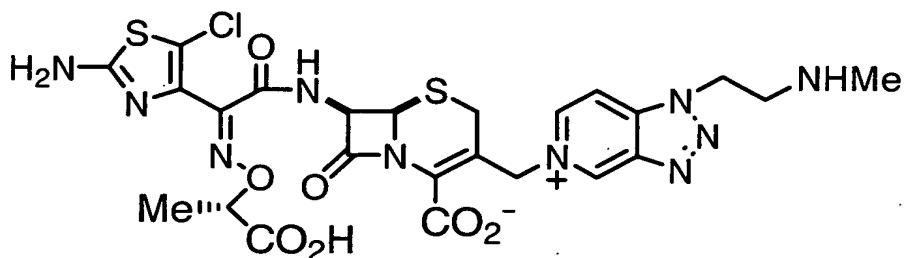
MS(ESI): 734⁺(M+H⁺).

Elementary Analysis as C₃₀H₃₆ClN₉O₇S₂ · 3.8 H₂O.

25 Calculated : C, 44.89 ; H, 5.47 ; N, 15.70 ; Cl, 4.42 ; S, 7.99 (%).

Found : C,44.79 ; H,5.22 ; N,15.82 ; Cl,4.32; S,7.89 (%).

Example 110



5 $^1\text{H-NMR}$ ($\text{D}_2\text{O}+\text{DCl}$) δ : 1.53 (3H, d, $J = 7.2$ Hz), 2.85 (3H, s), 3.39 and 3.80 (2H, ABq, $J = 18.6$ Hz), 3.88 (2H, t, $J = 5.7$ Hz), 4.97 (1H, q, $J = 7.2$ Hz), 5.31 (2H, t, $J = 5.7$ Hz), 5.37 (1H, d, $J = 4.7$ Hz), 5.54-6.00 (2H, m), 5.95 (1H, d, $J = 4.7$ Hz), 8.50 (1H, d, $J = 7.2$ Hz), 8.96 (1H, d, $J = 7.2$ Hz), 10.16(1H, s).

IR (KBr) cm^{-1} : 3407, 1774, 1609, 1539, 1483, 1447, 1394, 1359, 1287, 1190,

10 1155, 1104, 1066, 1034.

MS(ESI): 665 $^+$ ($\text{M}+\text{H}^+$).

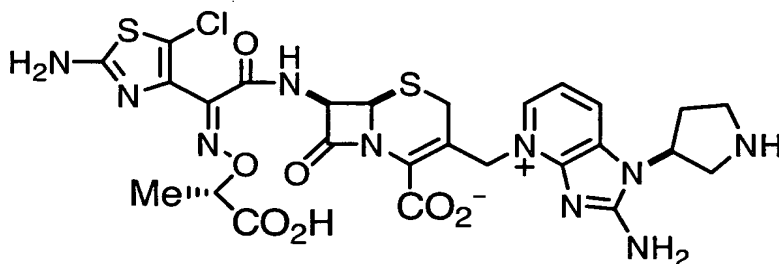
Elementary Analysis as $\text{C}_{24}\text{H}_{25}\text{ClN}_{10}\text{O}_7\text{S}_2 \cdot 3.2 \text{ H}_2\text{O}$.

Calculated : C,39.88 ; H,4.38; N,19.38 ; Cl,4.91; S,8.87 (%).

Found : C,39.93 ; H,4.02 ; N,19.34; Cl,4.76; S,8.64 (%).

15

Example 111



15 $^1\text{H-NMR}$ ($\text{D}_2\text{O}+\text{DCl}$) δ : 1.55 (3H, d, $J = 7.2$ Hz), 2.68 (2H, m), 3.36 and 3.60 (2H, ABq, $J = 18.6$ Hz), 3.57 and 3.97 (4H, m), 4.99 (1H, m), 5.29 (1H, d, $J = 5.0$ Hz), 5.50 and 5.69 (2H, ABq, $J =$
20 15.2 Hz), 5.92 (1H, d, $J = 5.0$ Hz), 7.34 (1H, t like), 8.06 (1H, d, $J = 7.5$ Hz), 8.16 (1H, d, $J = 6.6$ Hz).

IR (KBr) cm^{-1} : 3410, 1771, 1606, 1556, 1491, 1440, 1396, 1363, 1319, 1224,

1167, 1092, 1034.

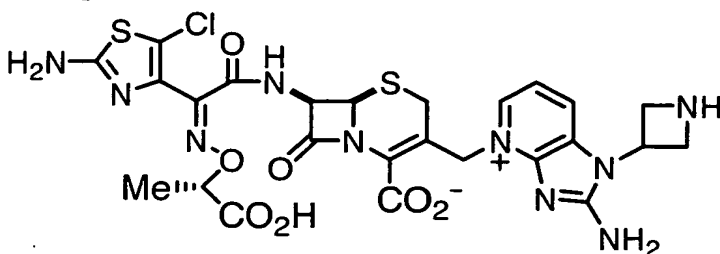
MS(FAB): 691 $^+$ ($\text{M}+\text{H}^+$).

25 Elementary Analysis as $\text{C}_{26}\text{H}_{27}\text{ClN}_{10}\text{O}_7\text{S}_2 \cdot 4.6 \text{ H}_2\text{O}$.

Calculated : C,40.35 ; H,4.71 ; N,18.10 ; Cl,4.58; S,8.29 (%).

Found : C,40.39 ; H,4.17 ; N,17.79 ; Cl,4.49; S,8.47 (%).

Example 112



¹H-NMR (D₂O+DCl) δ : 1.55 (3H, d, J = 7.5 Hz), 3.38 and 3.61 (2H, ABq, J = 18.6 Hz), 4.59-4.68 (2H, m), 4.92-5.03 (2H, m), 5.29 (1H, d, J = 4.8 Hz), 5.51 (1H, d, J = 15.0 Hz), 5.67-5.78 (2H, m), 5.92 (1H, d, J = 4.8 Hz), 7.40 (1H, dd, J = 6.6, 8.1 Hz), 8.21 (1H, d, J = 6.6 Hz), 8.29 (1H, d, J = 8.1 Hz).

IR (KBr) cm⁻¹: 3379, 1770, 1667, 1603, 1559, 1491, 1442, 1398, 1364, 1317, 1287, 1226, 1170, 1092, 1034.

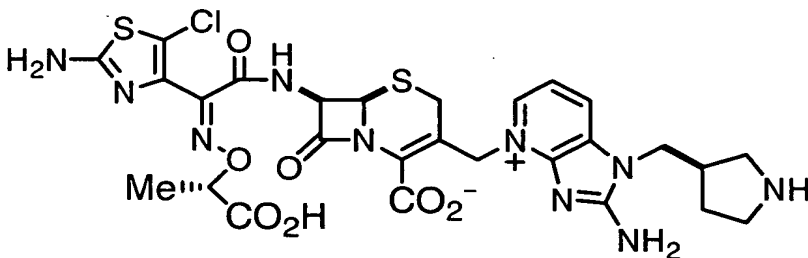
MS(ESI): 677⁺ (M+H)⁺.

Elementary Analysis as C₂₅H₂₅ClN₁₀O₇S₂ · 3.9H₂O.

Calculated : C,40.18; H,4.42; N,18.74; Cl,4.74; S,8.58 (%).

Found : C,40.36; H,4.32; N,18.37; Cl,4.76; S,8.39 (%).

Example 113



¹H-NMR (D₂O+DCl) δ : 1.55 (3H, d, J = 7.2 Hz), 1.83-2.37 (4H, m), 3.29-3.62 (4H, m), 4.07 (1H, m), 4.58 (2H, d, J = 7.2 Hz), 4.97 (1H, q, J = 7.2 Hz), 5.27 (1H, d, J = 5.0 Hz), 5.46 and 5.71 (2H, ABq, J = 15.3 Hz), 5.91 (1H, d, J = 5.0 Hz), 7.35 (1H, t-like), 8.02 (1H, d, J = 7.8 Hz), 8.17 (1H, d, J = 6.6 Hz).

IR (KBr) cm⁻¹: 3417, 1772, 1650, 1605, 1563, 1494, 1394, 1362, 1317, 1222, 1167, 1093, 1033.

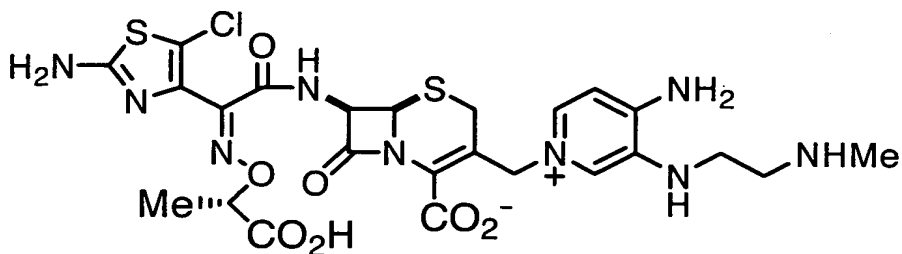
MS(ESI): 705⁺ (M+H)⁺.

Elementary Analysis as C₂₇H₂₉ClN₁₀O₇S₂ · 4.1 H₂O.

Calculated : C,41.63 ; H,4.81 ; N,17.98 ; Cl,4.55; S,8.23 (%).

Found : C,41.73 ; H,4.66 ; N,17.70 ; Cl,4.74; S,8.37 (%).

Example 114



5

¹H-NMR (D₂O) δ : 1.44 (3H, d, J = 6.9 Hz), 2.75 (3H, s), 3.11 and 3.57 (2H, ABq, J = 17.7 Hz), 3.32 (2H, t, J = 5.9 Hz), 3.51 (2H, t, J = 5.9 Hz), 4.66 (1H, q, J = 6.9 Hz), 4.77 and 5.12 (2H, ABq, J = 14.4 Hz), 5.24 (1H, d, J = 4.8 Hz), 5.69 (1H, d, J = 4.8 Hz), 6.83 (1H, d, J = 6.3 Hz), 7.86-7.89 (2H, m).

10 IR (KBr) cm⁻¹: 3371, 1773, 1600, 1546, 1492, 1457, 1394, 1358, 1284, 1185, 1157, 1093, 1066, 1034.

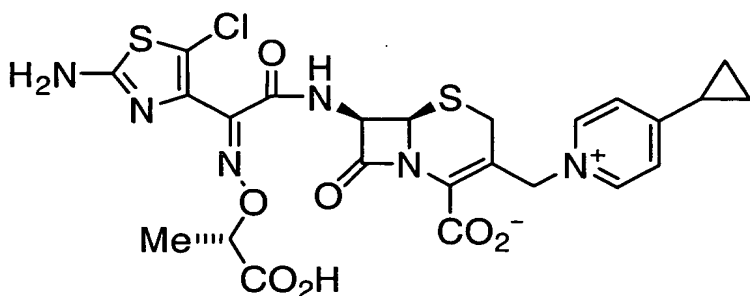
MS(FAB): 654⁺ (M+H)⁺.

Elementary Analysis as C₂₄H₂₈ClN₉O₇S₂ · 2.7H₂O.

Calculated : C,41.02; H,4.73; N,17.94; Cl,5.04; S,9.13 (%).

15 Found : C,41.14; H,4.53; N,17.91; Cl,4.73; S,8.55 (%).

Example 115



¹H-NMR (d₆-DMSO) δ : 1.07-1.18 (2H, m), 1.38 (3H, d, J = 7.2 Hz), 1.38-1.47 (2H, m), 2.20-2.38 (1H, m), 3.02 (1H, d, J = 17.7 Hz), 3.48 (1H, d, J = 17.7 Hz), 4.55 (1H, q, J = 7.2 Hz), 4.99 (1H, d, J = 13.2 Hz), 5.05 (1H, d, J = 4.2 Hz), 5.52 (1H, d, J = 13.2 Hz), 5.70 (1H, dd, J = 4.2, 8.4 Hz), 7.37-7.57 (2H, m), 7.82 (2H, d, J = 6.0 Hz), 9.19 (2H, d, J = 6.0 Hz), 9.58-9.73 (1H, m).

IR (KBr) cm⁻¹: 3409, 3053, 1778, 1674, 1637, 1538, 1518, 1475, 1453, 1389,

25 1353, 1215, 1185, 1158, 1100, 1034.

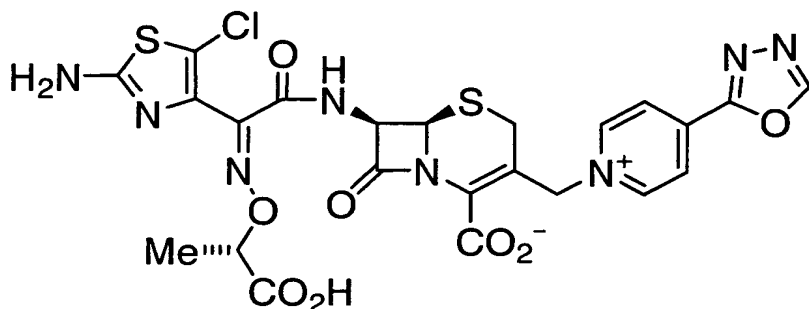
MS(FAB): 607⁺(M+H⁺).

Elementary Analysis as C₂₄H₂₃ClN₆O₇S₂·1.9 H₂O.

Calculated : C,44.95 ; H,4.21 ; N,13.10 ; Cl,5.53 ; S,10.00 (%).

Found : C,44.93 ; H,4.35 ; N,13.09 ; Cl,5.44 ; S,10.08 (%).

5 Example 116



¹H-NMR (d₆-DMSO) δ : 1.37 (3H, d, J = 6.9 Hz), 3.11 (1H, d, J = 17.7 Hz), 3.53 (1H, d, J = 17.7 Hz), 4.54 (1H, q, J = 6.9 Hz), 5.07 (1H, d, J = 4.8 Hz), 5.21 (1H, d, J = 13.8 Hz), 5.72 (1H, dd, J = 4.8, 8.4 Hz), 5.77 (1H, d, J = 13.8 Hz), 7.41 (2H, s), 8.73 (2H, d, J = 6.9 Hz), 9.51-9.82 (3H, m).

IR (KBr) cm⁻¹: 3413, 1777, 1671, 1615, 1538, 1510, 1457, 1391, 1346, 1237, 1189, 1152, 1103, 1083, 1035.

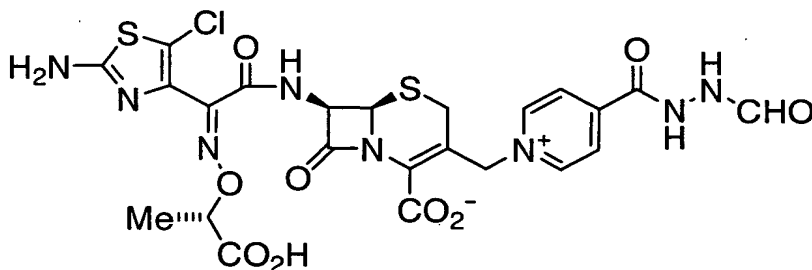
MS(FAB): 635⁺(M+H⁺).

Elementary Analysis as C₂₃H₁₉ClN₈O₈S₂·3.1 H₂O.

Calculated : C,39.98 ; H,3.68 ; N,16.22 ; Cl,5.13 ; S,9.28 (%).

Found : C,39.83 ; H,3.62 ; N,16.25 ; Cl,5.25 ; S,9.78 (%).

Example 117



¹H-NMR (d₆-DMSO) δ : 1.37 (3H, d, J = 6.9 Hz), 3.12 (1H, d, J = 18.0 Hz), 3.50 (1H, d, J = 18.0 Hz), 4.55 (1H, q, J = 6.9 Hz), 5.06 (1H, d, J = 5.1 Hz), 5.19 (1H, d, J = 13.2 Hz), 5.68-5.79 (2H, m), 7.41 (2H, s), 8.16 (1H, s), 8.46 (2H, d, J = 6.6 Hz), 9.49-9.75 (3H, m).

IR (KBr) cm⁻¹: 3287, 3196, 3055, 2988, 1779, 1673, 1618, 1538, 1457, 1345, 1242, 1188, 1119, 1065, 1035.

MS(FAB): 653⁺(M+H⁺).

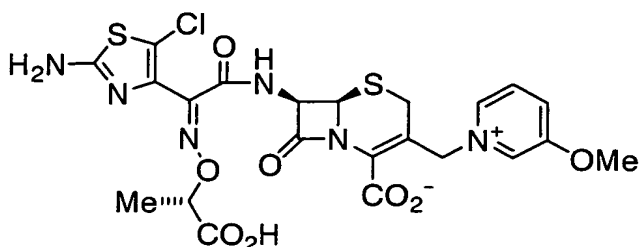
Elementary Analysis as C₂₃H₂₁ClN₈O₉S₂·2.1 H₂O.

Calculated : C,39.98 ; H,3.68 ; N,16.22 ; Cl,5.13 ; S,9.28 (%).

Found : C,39.97 ; H,3.75 ; N,16.57 ; Cl,4.72 ; S,8.79 (%).

5

Example 118



¹H-NMR (d₆-DMSO) δ : 1.38 (3H, d, J = 6.9 Hz), 3.08 (1H, d, J = 17.7 Hz), 3.50 (1H, d, J = 17.7 Hz), 3.99 (3H, s), 4.55 (1H, q, J = 6.9 Hz), 5.06 (1H, d, J = 4.5 Hz), 5.08 (1H, d, J = 12.9 Hz), 5.62 (1H, d, J = 12.9 Hz), 5.71 (1H, dd, J = 4.5, 8.1 Hz), 7.41 (2H, s), 8.08 (1H, dd, J = 5.7, 8.7 Hz), 8.22 (1H, d, J = 8.7 Hz), 9.11 (1H, d, J = 5.7 Hz), 9.41 (1H, s), 9.54-9.66 (1H, m).

IR (KBr) cm⁻¹: 3410, 2942, 1778, 1674, 1618, 1539, 1509, 1444, 1389, 1340, 1290, 1235, 1188, 1148, 1099, 1041, 1009.

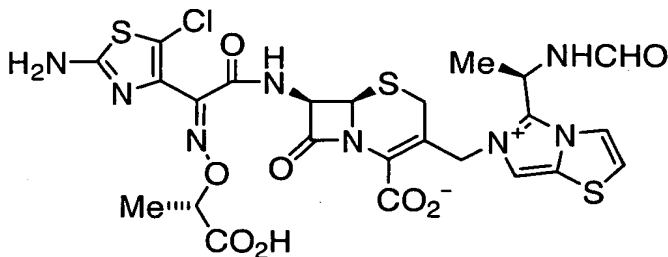
MS(FAB): 597⁺(M+H⁺).

Elementary Analysis as C₂₂H₂₁ClN₆O₈S₂·2.7 H₂O.

Calculated : C,40.92 ; H,4.12 ; N,13.02 ; Cl,5.49 ; S,9.93 (%).

Found : C,40.94 ; H,4.01 ; N,13.12 ; Cl,5.36 ; S,9.91 (%).

20 Example 119



¹H-NMR (d₆-DMSO) δ : 1.39 (3H, d, J = 7.2 Hz), 1.59 (3H, d, J = 7.2 Hz), 3.09 (1H, d, J = 17.4 Hz), 4.54 (1H, q, J = 7.2 Hz), 5.00 (1H, d, J = 5.4 Hz), 5.30 (1H, d, J = 13.8 Hz), 5.42 (1H, d, J = 13.8 Hz), 5.55-5.67 (1H, m), 5.72 (1H, dd, J = 5.4, 8.4 Hz), 7.41 (2H, s), 7.79 (1H, d, J = 4.2 Hz), 8.02-8.09 (2H, m), 8.30-8.39 (1H, m), 9.75 (1H, s).

IR (KBr) cm⁻¹: 3410, 2353, 1775, 1669, 1612, 1537, 1447, 1382, 1319, 1289,

1237, 1185, 1152, 1098, 1068, 1034.

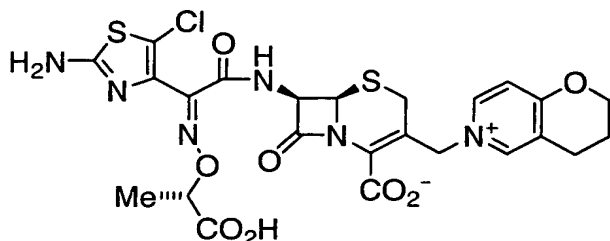
MS(FAB): 683⁺(M+H⁺).

Elementary Analysis as C₂₄H₂₃ClN₈O₈S₃·4.0 H₂O.

Calculated : C,38.17 ; H,4.14 ; N,14.84 ; Cl,4.69 ; S,12.74 (%).

5 Found : C,38.05 ; H,4.10 ; N,14.78 ; Cl,4.97 ; S,12.98 (%).

Example 120



¹H-NMR (d₆-DMSO) δ : 1.38 (3H, d, J = 6.6 Hz), 1.96-2.10 (2H, m), 2.79-2.90 (2H, m),
10 3.03 (1H, d, J = 17.7 Hz), 3.47 (1H, d, J = 17.7 Hz), 4.45-4.54 (2H, m), 4.54 (1H, q, J =
6.6 Hz), 4.86 (1H, d, J = 13.5 Hz), 5.04 (1H, d, J = 4.8 Hz), 5.43 (1H, d, J = 13.5 Hz), 5.70
(1H, dd, J = 4.8, 8.4 Hz), 7.38-7.48 (3H, m), 9.04 (1H, s), 9.08 (1H, d, J = 6.9 Hz), 9.64-
9.82 (1H, m).

IR (KBr) cm⁻¹: 3412, 3057, 1779, 1674, 1641, 1538, 1516, 1489, 1468, 1444,
15 1351, 1287, 1220, 1168, 1135, 1034, 1008.

MS(FAB): 623⁺(M+H⁺).

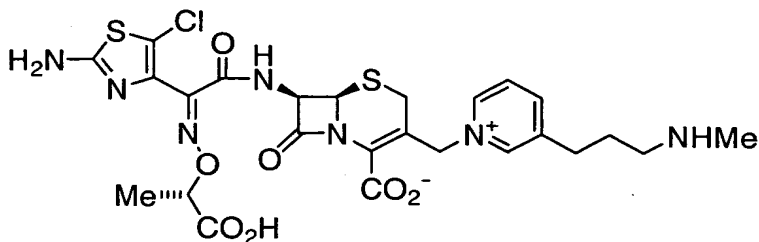
Elementary Analysis as C₂₄H₂₃ClN₆O₈S₂·2.0 H₂O.

Calculated : C,43.74 ; H,4.13 ; N,12.75 ; Cl,5.38 ; S,9.73 (%).

Found : C,43.71 ; H,3.94 ; N,12.94 ; Cl,5.13 ; S,9.49 (%).

20

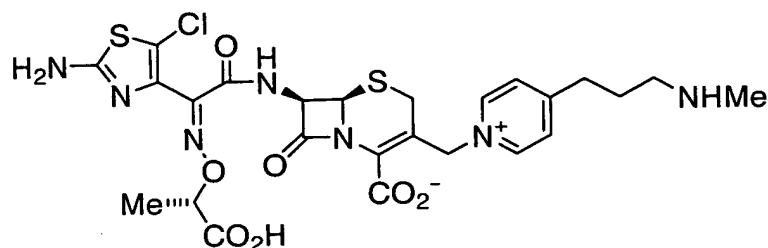
Example 121



¹H-NMR (D₂O) δ : 1.45 (3H, d, J = 7.2), 2.09 (2H, m), 2.71 (3H, s), 2.97 (2H, t, J = 8.1
Hz), 3.10 (2H, t, J = 8.1 Hz), 3.16 (1H, d, J = 18.0 Hz), 3.65 (1H, d, J = 18.0 Hz), 4.66
25 (1H, q, J = 7.2 Hz), 5.25 (1H, d, J = 14.1 Hz), 5.28 (1H, d, J = 5.1 Hz), 5.56 (1H, d, J =
14.1 Hz), 5.88 (1H, d, J = 5.1 Hz), 8.01 (1H, dd, J = 6.6, 7.5 Hz), 8.45 (1H, d, J = 7.5 Hz),
8.82 (1H, d, J = 6.6 Hz), 8.93 (1H, brs).

Found : C, 42.27; H, 5.09; N, 13.80; Cl, 5.00; S, 9.08 (%).

Example 122



10 ¹H-NMR (D₂O) δ: 1.36 (3H, d, J = 6.9), 2.04 (2H, m), 2.64 (3H, s), 2.95 (2H, t, J = 7.8 Hz), 3.03 (2H, t, J = 7.8 Hz), 3.11 (1H, d, J = 17.7 Hz), 3.55 (1H, d, J = 17.7 Hz), 4.58 (1H, q, J = 6.9 Hz), 5.17 (1H, d, J = 14.7 Hz), 5.19 (1H, d, J = 4.8 Hz), 5.45 (1H, d, J = 14.7 Hz), 5.81 (1H, d, J = 4.8 Hz), 7.86 (2H, d, J = 6.9 Hz), 8.76 (2H, d, J = 6.9 Hz).

IR (KBr) cm^{-1} : 3397, 2821, 1776, 1606, 1538, 1467, 1394, 1350, 1287, 1231,

15 1187, 1152, 1094, 1066, 1033.

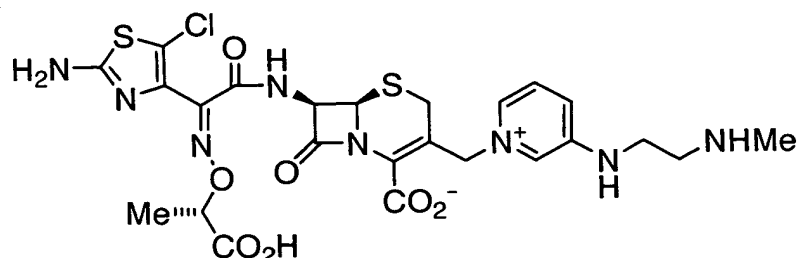
MS (ESI): 638 (M+H)⁺, 660 (M+Na)⁺.

Elementary Analysis as $\text{C}_{25}\text{H}_{28}\text{ClN}_7\text{O}_7\text{S}_2 \cdot 3.8 \text{H}_2\text{O}$.

Calculated : C, 42.50; H, 5.08; N, 13.88; Cl, 5.02; S, 9.08 (%).

Found : C, 42.34; H, 5.10; N, 13.97; Cl, 5.07; S, 9.29 (%).

Example 123



¹H-NMR (d₆-DMSO) δ : 1.41 (3H, d, J = 6.9 Hz), 2.48 (3H, s), 2.81 (1H, d, J = 17.4 Hz), 2.94-3.06 (2H, m), 3.30-3.40 (2H, m), 3.50 (1H, d, J = 17.4 Hz), 4.47 (1H, q, J = 6.9 Hz), 4.87 (1H, d, J = 13.2 Hz), 5.12 (1H, d, J = 5.4 Hz), 5.41 (1H, d, J = 13.2 Hz), 5.82 (1H, dd,

J = 5.4, 9.0 Hz), 7.35 (2H, s), 7.58-7.74 (3H, m), 8.23-8.32 (1H, m), 9.11 (1H, s), 11.10-11.23 (1H, m).

IR (KBr) cm^{-1} : 3362, 3086, 1774, 1593, 1539, 1511, 1458, 1394, 1353, 1288, 1184, 1154, 1095, 1065, 1033.

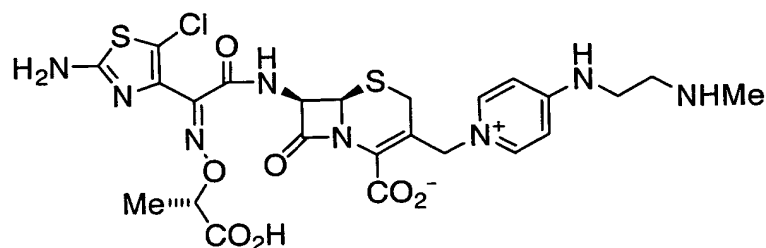
5 MS(ESI): 639⁺(M+H⁺).

Elementary Analysis as $\text{C}_{24}\text{H}_{27}\text{ClN}_8\text{O}_7\text{S}_2 \cdot 3.0 \text{ H}_2\text{O}$.

Calculated : C,41.59 ; H,4.80 ; N,16.17 ; Cl,5.11 ; S,9.25 (%).

Found : C,41.54 ; H,4.67 ; N,16.18 ; Cl,5.17 ; S,9.45 (%).

10 Example 124



¹H-NMR (D_2O) δ : 1.45 (3H, d, J = 6.9 Hz), 2.76 (3H, s), 3.17 (1H, d, J = 18.0 Hz), 3.33 (2H, t, J = 6.0 Hz), 3.58 (1H, d, J = 18.0 Hz), 3.75 (2H, t, J = 6.0 Hz), 4.66 (1H, q, J = 6.9 Hz), 4.89 (1H, d, J = 14.7 Hz), 5.09 (1H, d, J = 14.7 Hz), 5.24 (1H, d, J = 4.8 Hz), 5.86 (1H, d, J = 4.8 Hz), 6.94 (2H, d, J = 6.3 Hz), 8.04-8.35 (2H, m).

15

IR (KBr) cm^{-1} : 3398, 3066, 1773, 1650, 1601, 1556, 1450, 1394, 1357, 1288, 1218, 1168, 1094, 1065, 1035.

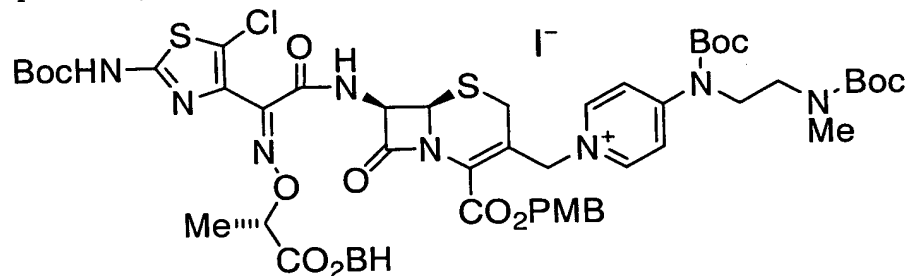
MS(FAB): 639⁺(M+H⁺).

Elementary Analysis as $\text{C}_{24}\text{H}_{27}\text{ClN}_8\text{O}_7\text{S}_2 \cdot 3.4 \text{ H}_2\text{O}$.

20 Calculated : C,41.16 ; H,4.86 ; N,16.00 ; Cl,5.06 ; S,9.16 (%).

Found : C,41.14 ; H,4.69 ; N,16.00 ; Cl,4.97 ; S,9.36 (%).

quaternary salt ester :



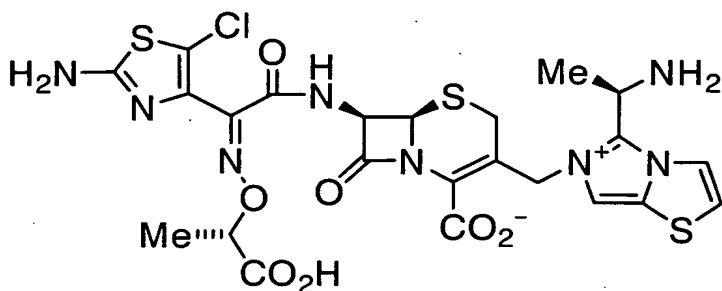
¹H-NMR ($\text{d}_6\text{-DMSO}$) δ : 1.15-1.40 (9H, m), 1.43-1.50 (12H, m), 1.54 (9H, s), 2.75-2.86 (3H, m), 3.20-3.38 (3H, m), 3.45 (1H, d, J = 17.7 Hz), 3.76 (3H, s), 4.00-4.16 (2H, m),

25

4.90 (1H, q, J = 6.9 Hz), 5.21 (1H, d, J = 12.6 Hz), 5.21 (1H, d, J = 5.1 Hz), 5.28 (1H, d, J = 12.6 Hz), 5.41 (2H, s), 5.97 (1H, dd, J = 5.1, 8.1 Hz), 6.83 (1H, s), 6.93 (2H, d, J = 8.1 Hz), 7.20-7.44 (12H, m), 8.09 (2H, d, J = 7.5 Hz), 8.73 (2H, d, J = 7.5 Hz), 9.73 (1H, d, J = 8.1 Hz), 12.08 (1H, s).

- 5 IR (KBr) cm^{-1} : 3425, 2978, 2934, 1793, 1724, 1693, 1638, 1613, 1551, 1516, 1479, 1455, 1393, 1369, 1249, 1223, 1153, 1065, 1036.
MS(FAB): 1225 $^{+}$ (M $^{+}$).

Example 125



$^1\text{H-NMR}$ (d_6 -DMSO) δ : 1.39 (3H, d, J = 6.9 Hz), 1.47 (3H, d, J = 6.6 Hz), 3.15 (1H, d, J = 17.4 Hz), 3.40 (3H, d, J = 17.4 Hz), 4.55 (1H, q, J = 6.9 Hz), 4.99-50.6 (2H, m), 5.27 (1H, d, J = 13.8 Hz), 5.42 (1H, d, J = 13.8 Hz), 5.71 (1H, dd, J = 5.1, 9.0 Hz), 7.41 (2H, br s), 7.70 (1H, d, J = 4.2 Hz), 8.06 (1H, m), 8.45 (1H, d, J = 4.2 Hz), 9.78 (1H, br s).

- 15 IR (KBr) cm^{-1} : 3394, 1773, 1670, 1613, 1537, 1446, 1354, 1183, 1152, 1094, 1066, 1035.

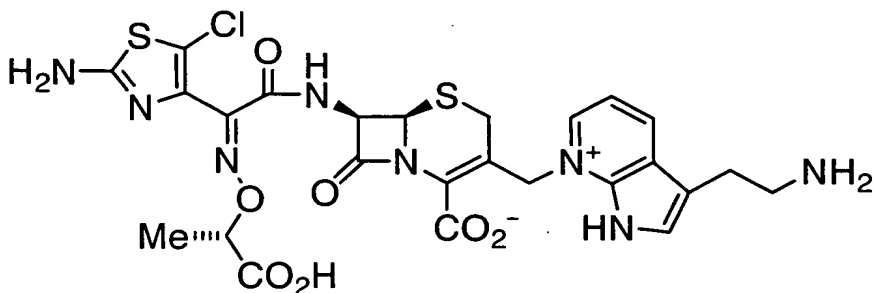
MS (FAB): 655 (M+H) $^{+}$, 1309 (2M+H) $^{+}$.

Elementary Analysis as $\text{C}_{23}\text{H}_{23}\text{ClN}_8\text{O}_7\text{S}_3 \cdot 3.6 \text{H}_2\text{O}$.

Calculated : C, 38.37; H, 4.23; N, 15.56; Cl, 4.92; S, 13.36 (%).

- 20 Found : C, 38.61; H, 4.01; N, 15.58; Cl, 4.92; S, 13.08 (%).

Example 126



$^1\text{H-NMR}$ (D_2O) δ : 1.38 (3H, d, J = 7.2), 2.89 (1H, d, J = 18.0 Hz), 3.17 (2H, t, J = 7.2 Hz), 3.33 (2H, t, J = 7.2 Hz), 3.70 (1H, d, J = 18.0 Hz), 4.62 (1H, q, J = 7.2 Hz), 5.20 (1H,

d, $J = 15.0$ Hz), 5.29 (1H, d, $J = 4.8$ Hz), 5.83 (1H, d, $J = 4.8$ Hz), 6.00 (1H, d, $J = 15.0$ Hz), 7.58 (1H, br t, $J = 7.5$ Hz), 7.64 (1H, s), 8.50 (1H, d, $J = 6.0$ Hz), 8.65 (1H, d, $J = 7.5$ Hz).

IR (KBr) cm^{-1} : 3396, 3184, 2821, 1772, 1598, 1539, 1445, 1384, 1361, 1288,

5 1219, 1188, 1157, 1093, 1061, 1035.

MS (FAB): 649 ($\text{M}+\text{H}$)⁺, 1297 ($2\text{M}+\text{H}$)⁺.

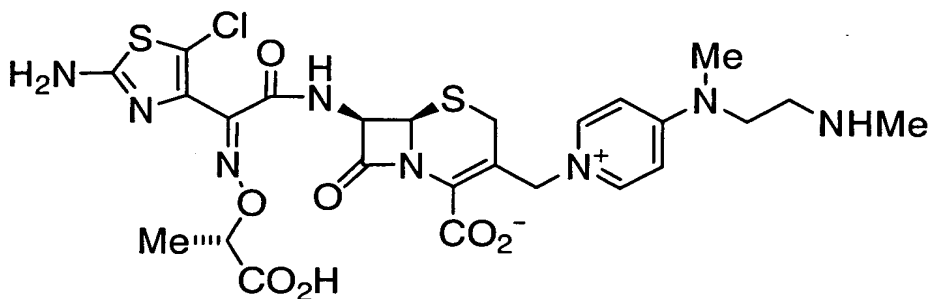
Elementary Analysis as $\text{C}_{25}\text{H}_{25}\text{ClN}_8\text{O}_7\text{S}_2 \cdot 3.8 \text{H}_2\text{O}$.

Calculated : C, 41.85; H, 4.58; N, 15.62; Cl, 4.94; S, 8.94 (%).

Found : C, 41.78; H, 4.34; N, 15.66; Cl, 4.98; S, 8.77 (%).

10

Example 127



15

¹H-NMR (D_2O) δ : 1.46 (3H, d, $J = 6.9$), 2.76 (3H, s), 3.18 (1H, d, $J = 18.0$ Hz), 3.23 (3H, s), 3.36 (2H, t, $J = 6.9$ Hz), 3.58 (1H, d, $J = 18.0$ Hz), 3.95 (2H, t, $J = 6.9$ Hz), 4.68 (1H, q, $J = 6.9$ Hz), 4.91 (1H, d, $J = 15.0$ Hz), 5.10 (1H, d, $J = 15.0$ Hz), 5.24 (1H, d, $J = 4.8$ Hz), 5.86 (1H, d, $J = 4.8$ Hz), 7.01 (2H, d, $J = 7.5$ Hz), 8.24 (2H, d, $J = 7.5$ Hz).

IR (KBr) cm^{-1} : 3408, 1775, 1650, 1606, 1556, 1450, 1404, 1359, 1286, 1235, 1164, 1106, 1064, 1034.

MS (FAB): 653 ($\text{M}+\text{H}$)⁺, 1305 ($2\text{M}+\text{H}$)⁺.

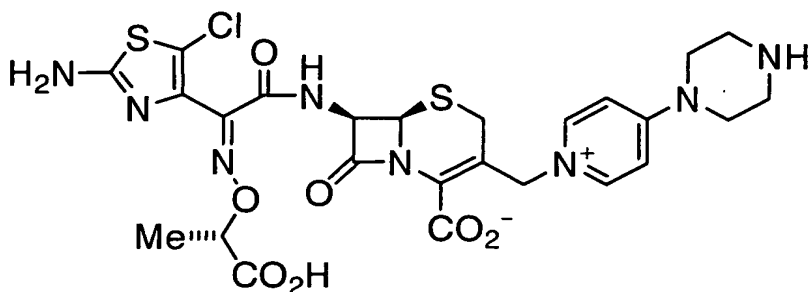
20

Elementary Analysis as $\text{C}_{25}\text{H}_{29}\text{ClN}_8\text{O}_7\text{S}_2 \cdot 3.7 \text{H}_2\text{O}$.

Calculated : C, 41.72; H, 5.10; N, 15.77; Cl, 4.93; S, 8.91 (%).

Found : C, 41.79; H, 4.94; N, 15.48; Cl, 4.92; S, 8.78 (%).

Example 128



¹H-NMR (D₂O) δ : 1.45 (3H, d, J = 6.9), 3.17 (1H, d, J = 18.0 Hz), 3.45 (4H, m), 3.58 (1H, d, J = 18.0 Hz), 3.97 (4H, m), 4.66 (1H, q, J = 6.9 Hz), 4.92 (1H, d, J = 15.0 Hz), 5.13 (1H, d, J = 15.0 Hz), 5.24 (1H, d, J = 4.8 Hz), 5.86 (1H, d, J = 4.8 Hz), 7.15 (2H, d, J = 7.8 Hz), 8.27 (2H, d, J = 7.8 Hz).

IR (KBr) cm⁻¹: 3398, 1771, 1649, 1603, 1544, 1450, 1385, 1362, 1283, 1239, 1175, 1151, 1093, 1065, 1035.

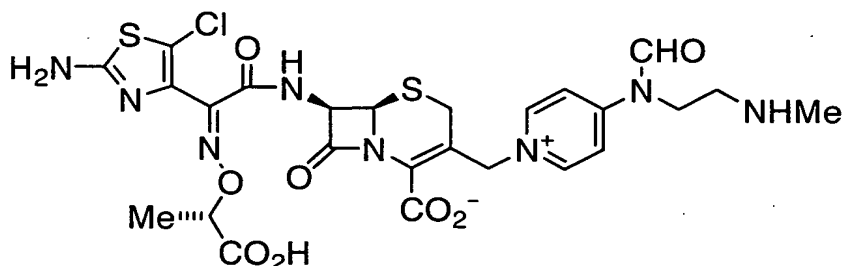
MS (ESI): 651 (M+H)⁺, 673 (M+Na)⁺.

Elementary Analysis as C₂₅H₂₇ClN₈O₇S₂·3.7 H₂O.

Calculated : C, 41.83; H, 4.83; N, 15.61; Cl, 4.94; S, 8.93 (%).

Found : C, 41.79; H, 4.72; N, 15.71; Cl, 4.97; S, 8.96 (%).

Example 129



¹H-NMR (D₂O) δ : 1.52 (3H, d, J = 7.2), 2.89 (3H/2, s), 3.04 (3H/2, s), 3.18 (1H, br d, J = 18.0 Hz), 3.52-3.62 (5H, m), 4.84 (1H, q, J = 7.2 Hz), 4.90 (1H, d, J = 15.0 Hz), 5.05 (1H, d, J = 15.0 Hz), 5.25 (1H, d, J = 4.8 Hz), 5.86 (1H, d, J = 4.8 Hz), 6.88 (2H, m), 7.88 (1H/2, s), 7.99 (1H/2, s), 8.02-8.19 (2H, m).

IR (KBr) cm⁻¹: 3406, 1778, 1650, 1554, 1446, 1391, 1352, 1219, 1170, 1096, 1064, 1034.

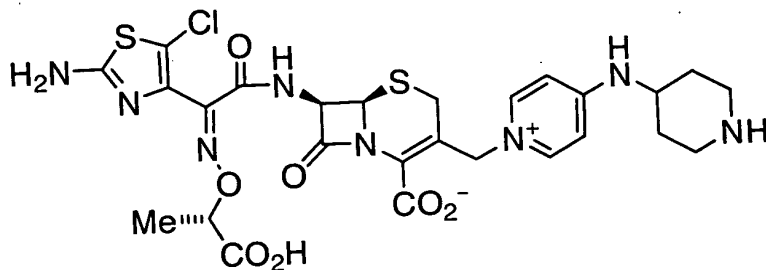
MS (ESI): 667 (M+H)⁺.

Elementary Analysis as C₂₅H₂₇ClN₈O₈S₂·2.7 H₂O.

Calculated : C, 41.95; H, 4.56; N, 15.66; Cl, 4.95; S, 8.96 (%).

Found : C, 41.93; H, 4.40; N, 15.73; Cl, 5.12; S, 8.93 (%).

Example 130



- ¹H-NMR (D₂O) δ : 1.44 (3H, d, J = 6.6 Hz), 1.69-1.90 (2H, m), 2.20-2.34 (2H, m), 3.09-3.25 (3H, m), 3.44-3.62 (3H, m), 3.84-4.00 (1H, m), 4.65 (1H, q, J = 6.6 Hz), 4.86 (1H, d, J = 14.7 Hz), 5.06 (1H, d, J = 14.7 Hz), 5.23 (1H, d, J = 5.1 Hz), 5.86 (1H, d, J = 5.1 Hz), 6.80-7.00 (2H, m), 7.96-8.28 (2H, m).

IR (KBr) cm⁻¹: 3395, 2527, 1773, 1650, 1594, 1553, 1453, 1387, 1287, 1217, 1166, 1097, 1066, 1034.

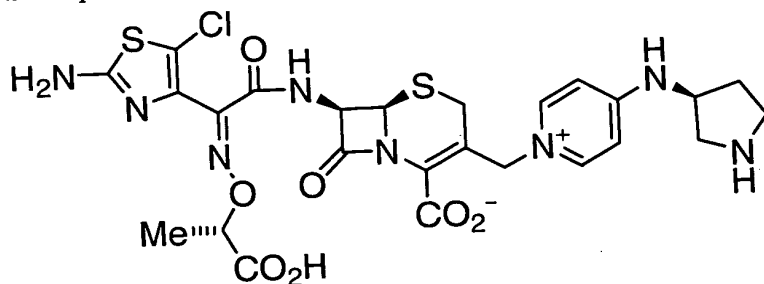
MS(FAB): 665⁺(M+H⁺).

- 10 Elementary Analysis as C₂₆H₂₉ClN₈O₇S₂·6.2 H₂O.

Calculated : C, 40.20 ; H, 5.37 ; N, 14.42 ; Cl, 4.56 ; S, 8.26 (%).

Found : C, 40.13 ; H, 5.07 ; N, 14.45 ; Cl, 4.81 ; S, 8.37 (%).

Example 131



- 15 ¹H-NMR (D₂O) δ : 1.56 (3H, d, J = 7.2 Hz), 2.13-2.25 (1H, m), 2.45-2.58 (1H, m), 3.28 and 3.64 (2H, ABq, J = 18.3 Hz), 3.36-3.77 (4H, m), 4.53-4.60 (1H, m), 4.96 (1H, q, J = 6.9 Hz), 4.99 and 5.25 (2H, ABq, J = 14.7 Hz), 5.30 (1H, d, J = 4.8 Hz), 5.90 (1H, d, J = 4.8 Hz), 6.82 (2H, d, J = 7.2 Hz), 8.18 (1H, m).

- 20 IR (KBr) cm⁻¹: 1773, 1650, 1597, 1551, 1446, 1391, 1286, 1217, 1167.

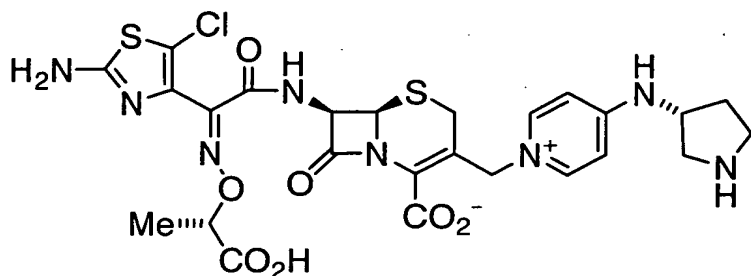
MS (ESI): 651 (M+H)⁺, 673 (M+Na)⁺.

Elementary Analysis as C₂₅H₂₇ClN₈O₇S₂·2.7 H₂O.

Calculated : C, 42.91; H, 4.67; N, 16.01; Cl, 5.07; S, 9.17 (%).

Found : C, 42.98; H, 4.64; N, 15.99; Cl, 4.97; S, 9.29 (%).

Example 132



$^1\text{H-NMR}$ (D_2O) δ : 1.56 (3H, d, $J = 7.2\text{Hz}$), 2.16-2.24 (1H, m), 2.46-2.58 (1H, m), 3.29 and 3.64 (2H, ABq, $J = 18.2\text{ Hz}$), 3.37-3.78 (4H, m), 4.53-4.60 (1H, m), 4.96 (1H, q, $J = 7.2\text{ Hz}$), 5.00 and 5.26 (2H, ABq, $J = 14.7\text{ Hz}$), 5.30 (1H, d, $J = 4.8\text{ Hz}$), 5.90 (1H, d, $J = 4.8\text{ Hz}$), 6.96 (2H, d, $J = 7.5\text{ Hz}$), 8.20 (1H, m).

IR (KBr) cm^{-1} : 1774, 1650, 1595, 1551, 1446, 1391, 1286, 1218, 1167.

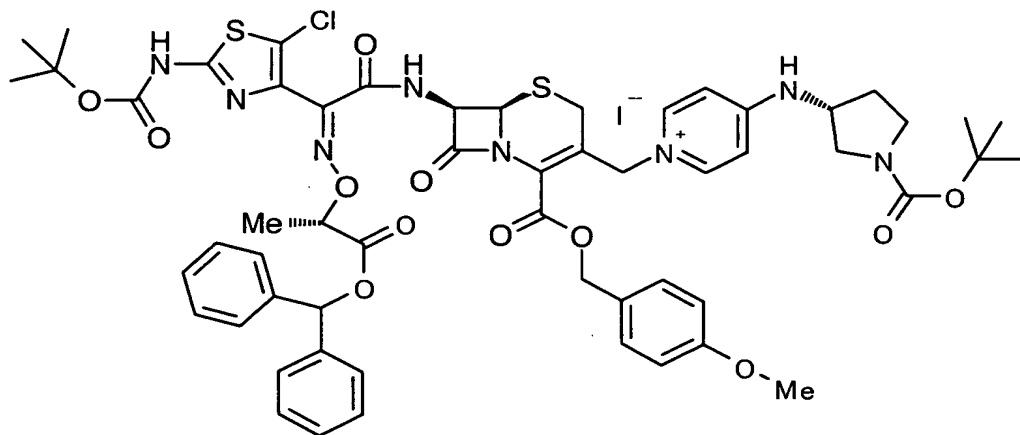
MS (ESI): 651 ($\text{M}+\text{H}$) $^+$, 673 ($\text{M}+\text{Na}$) $^+$.

Elementary Analysis as $\text{C}_{25}\text{H}_{27}\text{ClN}_8\text{O}_7\text{S}_2 \cdot 2.2\text{ H}_2\text{O}$.

10 Calculated : C, 43.47; H, 4.58; N, 16.22; Cl, 5.13; S, 9.28 (%).

Found : C, 43.40; H, 4.60; N, 16.25; Cl, 5.07; S, 9.28 (%).

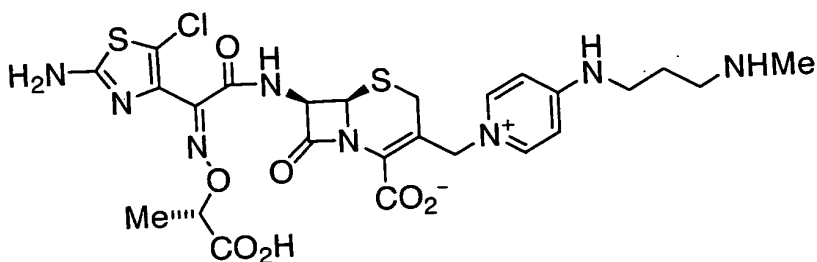
quaternary salt ester :



15 $^1\text{H-NMR}$ (DMSO) δ : 1.41 (9H, s), 1.46-1.48 (12H, m), 1.78-1.96 (1H, m), 2.10-2.30 (1H, m), 3.11-3.25 (1H, m), 3.37, 3.49 (ABq, $J=18.9\text{Hz}$), 3.54-3.76 (2H, m), 3.76 (3H, s), 4.19-4.36 (1H, m), 4.90 (1H, q, $J = 6.9\text{ Hz}$), 5.04-5.15 (2H, m), 5.20 (1H, d, $J=5.1\text{Hz}$), 5.21, 5.26 (2H, ABq, $J=11.7\text{Hz}$), 5.96 (1H, dd, $J=4.8\text{Hz}$, $J=8.1\text{Hz}$), 6.84 (1H, s), 6.86-6.97 (4H, m), 7.07 (1H, d, $J=7.8\text{Hz}$), 7.19, 7.48 (10H, m), 8.07, 8.09 (1H, m), 8.27 (1H, d, $J=7.5\text{Hz}$), 8.92, 8.94 (1H, m), 9.74 (1H, $J=8.4\text{Hz}$), 12.11 (1H, s).

20

Example 133



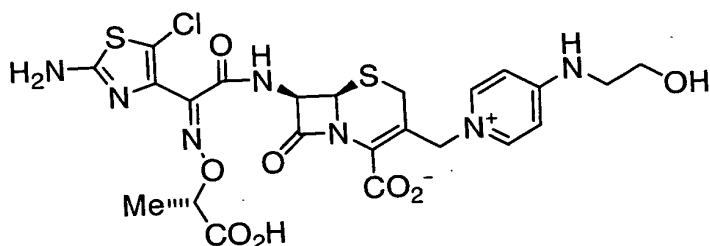
¹H-NMR (D₂O) δ : 1.45 (3H, d, J = 6.9), 2.04 (3H, m), 2.72 (3H, s), 3.12 (2H, t, J = 7.8 Hz), 3.16 (1H, d, J = 18.0 Hz), 3.44 (2H, t, J = 6.9 Hz), 3.56 (1H, d, J = 18.0 Hz), 4.66 (1H, q, J = 6.9 Hz), 4.86 (1H, d, J = 14.4 Hz), 5.05 (1H, d, J = 14.4 Hz), 5.23 (1H, d, J = 4.8 Hz), 5.86 (1H, d, J = 4.8 Hz), 6.85 (2H, d, J = 7.5 Hz), 8.02-8.18 (2H, m).
 IR (KBr) cm⁻¹: 3397, 1773, 1651, 1598, 1556, 1462, 1395, 1360, 1288, 1216, 1168, 1093, 1065, 1034.

MS (ESI): 653 (M+H)⁺, 675 (M+Na)⁺.

Elementary Analysis as C₂₅H₂₉ClN₈O₇S₂·3.8 H₂O.

10 Calculated : C, 41.61; H, 5.11; N, 15.53; Cl, 4.91; S, 8.89 (%).
 Found : C, 41.47; H, 5.08; N, 15.63; Cl, 5.15; S, 8.98 (%).

Example 134



15 ¹H-NMR (d₆-DMSO) δ : 1.39 (3H, d, J = 6.9), 2.97 (1H, d, J = 18.0 Hz), 3.34 (2H, m), 3.46 (1H, d, J = 18.0 Hz), 3.59 (2H, t, J = 5.1 Hz), 4.56 (1H, q, J = 6.9 Hz), 4.65 (1H, d, J = 13.5 Hz), 5.05 (1H, d, J = 4.8 Hz), 5.16 (1H, d, J = 13.5 Hz), 5.70 (1H, dd, J = 4.8, 8.4 Hz), 6.94 (2H, m), 7.41 (2H, br s), 8.44 (1H, d, J = 6.9 Hz), 8.59 (1H, d, J = 7.5 Hz), 8.85 (1H, 5.4 Hz), 9.65 (1H, br).

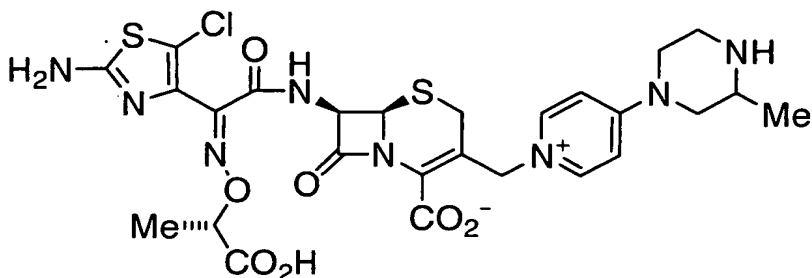
20 IR (KBr) cm⁻¹: 3398, 1776, 1651, 1555, 1450, 1378, 1350, 1218, 1171, 1097, 1063, 1035.

MS (ESI): 626 (M+H)⁺, 1251 (2M+H)⁺.

Elementary Analysis as C₂₃H₂₄ClN₇O₈S₂·2.3 H₂O.

25 Calculated : C, 41.39; H, 4.32; N, 14.69; Cl, 5.31; S, 9.61 (%).
 Found : C, 41.39; H, 4.34; N, 14.78; Cl, 5.11; S, 9.37 (%).

Example 135



¹H-NMR (D₂O) δ : 1.40 (3H, d, J = 6.3), 1.45 (3H, d, J = 6.9 Hz), 3.17 (1H, d, J = 18.0 Hz), 3.34 (1H, m), 3.55-3.61 (4H, m), 4.28-4.33 (2H, m), 4.66 (1H, q, J = 6.9 Hz), 4.91 (1H, d, J = 14.7 Hz), 5.12 (1H, d, J = 14.7 Hz), 5.24 (1H, d, J = 4.8 Hz), 5.86 (1H, d, J = 4.8 Hz), 7.16 (2H, d, J = 7.2 Hz), 8.27 (2H, d, J = 7.2 Hz).

IR (KBr) cm⁻¹: 3408, 1773, 1649, 1605, 1546, 1449, 1386, 1360, 1284, 1239, 1158, 1107, 1065, 1036.

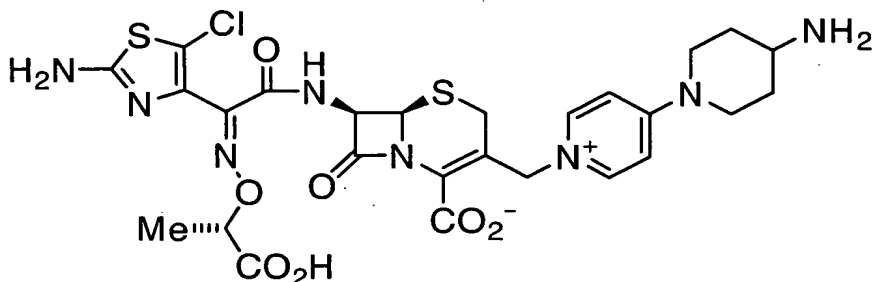
MS (ESI): 665 (M+H)⁺, 687 (M+Na)⁺.

Elementary Analysis as C₂₆H₂₉ClN₈O₇S₂·4.5 H₂O.

Calculated : C, 41.85; H, 5.13; N, 15.02; Cl, 4.75; S, 8.59 (%).

Found : C, 41.86; H, 4.84; N, 15.06; Cl, 4.74; S, 8.48 (%).

Example 136



¹H-NMR (D₂O) δ : 1.32 (3H, d, J = 6.9), 1.57 (2H, m), 2.08 (2H, m), 3.04 (1H, d, J = 17.4 Hz), 3.15 (2H, m), 3.48 (1H, m), 4.14 (2H, m), 4.53 (1H, q, J = 6.9 Hz), 4.74 (1H, d, J = 15.0 Hz), 4.94 (1H, d, J = 15.0 Hz), 5.12 (1H, d, J = 4.8 Hz), 5.73 (1H, d, J = 4.8 Hz), 6.96 (2H, d, J = 7.2 Hz), 8.02 (2H, d, J = 7.2 Hz).

IR (KBr) cm⁻¹: 3398, 1772, 1650, 1600, 1549, 1451, 1389, 1362, 1286, 1238, 1174, 1095, 1065, 1035.

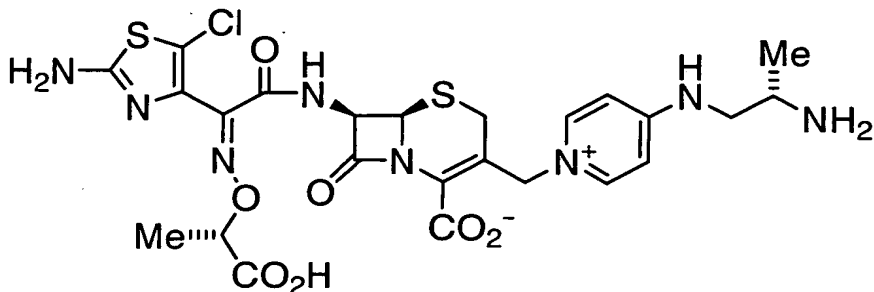
MS (ESI): 665 (M+H)⁺, 687 (M+Na)⁺.

Elementary Analysis as C₂₆H₂₉ClN₈O₇S₂·4.3 H₂O.

Calculated : C, 42.05; H, 5.10; N, 15.09; Cl, 4.77; S, 8.64 (%).

Found : C, 42.12; H, 5.16; N, 14.95; Cl, 4.68; S, 8.50 (%).

Example 137



¹H-NMR (D₂O) δ : 1.36 (3H, d, J = 6.3 Hz), 1.45 (3H, d, J = 6.6 Hz), 3.17 (1H, d, J = 18.0 Hz), 3.57 (1H, d, J = 18.0 Hz), 3.58-3.72 (3H, m), 4.65 (1H, q, J = 6.6 Hz), 4.87 (1H, d, J = 14.4 Hz), 5.09 (1H, d, J = 14.4 Hz), 5.23 (1H, d, J = 5.1 Hz), 5.86 (1H, d, J = 5.1 Hz), 6.93 (2H, d, J = 6.9 Hz), 8.05-8.38 (2H, m).

IR (KBr) cm⁻¹: 3294, 2983, 1774, 1650, 1592, 1555, 1456, 1395, 1360, 1287,

1218, 1167, 1092, 1065, 1034.

MS(ESI): 639⁺(M+H⁺).

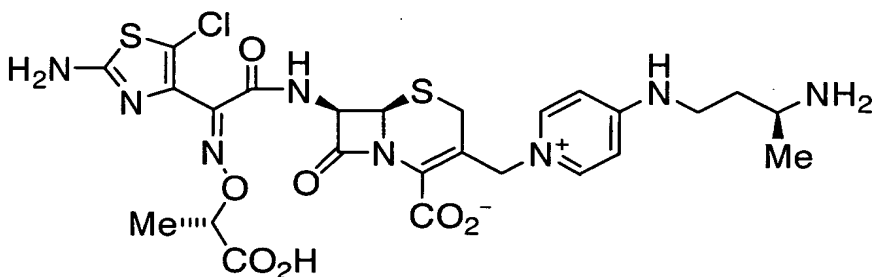
Elementary Analysis as C₂₄H₂₇ClN₈O₇S₂·2.8 H₂O.

Calculated : C, 41.80 ; H, 4.77 ; N, 16.25 ; Cl, 5.14 ; S, 9.30 (%).

Found : C, 41.83 ; H, 4.64 ; N, 16.29 ; Cl, 4.96 ; S, 9.22 (%).

15

Example 138



¹H-NMR (D₂O) δ : 1.35 (3H, d, J = 6.3 Hz), 1.45 (3H, d, J = 6.6 Hz), 1.82-2.13 (2H, m), 3.16 (1H, d, J = 17.7 Hz), 3.35-3.50 (3H, m), 3.55 (1H, d, J = 17.7 Hz), 4.65 (1H, q, J = 6.6 Hz), 4.83 (1H, d, J = 14.4 Hz), 5.05 (1H, d, J = 14.4 Hz), 5.22 (1H, d, J = 4.2 Hz), 5.85 (1H, d, J = 4.2 Hz), 6.83 (2H, d, J = 6.3 Hz), 7.95-8.25 (2H, m).

IR (KBr) cm⁻¹: 3415, 3067, 2982, 1772, 1650, 1597, 1557, 1447, 1395, 1360,

1288, 1216, 1169, 1094, 1065, 1034.

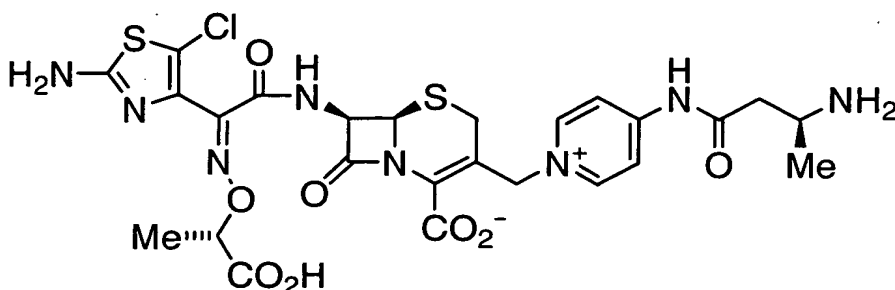
MS(FAB): 653⁺(M+H⁺).

25 Elementary Analysis as C₂₅H₂₉ClN₈O₇S₂·3.6 H₂O.

Calculated : C,41.82 ; H,5.08 ; N,15.61 ; Cl,4.94 ; S,8.93 (%).

Found : C,41.89 ; H,4.95 ; N,15.54 ; Cl,4.57 ; S,8.60 (%).

Example 139



5

$^1\text{H-NMR}$ (D_2O) δ : 1.40 (3H, d, $J = 6.6$ Hz), 1.44 (3H, d, $J = 6.9$ Hz), 2.88-3.02 (2H, m), 3.17 (1H, d, $J = 17.7$ Hz), 3.63 (1H, d, $J = 17.7$ Hz), 3.88 (1H, m), 4.66 (1H, q, $J = 6.9$ Hz), 5.13 (1H, d, $J = 14.7$ Hz), 5.26 (1H, d, $J = 5.1$ Hz), 5.40 (1H, d, $J = 14.4$ Hz), 5.87 (1H, d, $J = 5.1$ Hz), 8.07 (2H, d, $J = 7.2$ Hz), 8.71 (2H, d, $J = 7.2$ Hz).

10 IR (KBr) cm^{-1} : 3388, 1775, 1716, 1607, 1537, 1517, 1464, 1394, 1328, 1287, 1182, 1159, 1101, 1066, 1035.

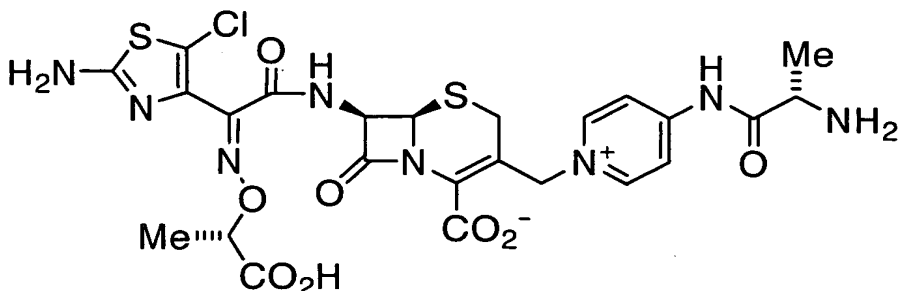
MS(FAB): 667 ($\text{M}+\text{H}$) $^+$, 1333 ($2\text{M}+\text{H}$) $^+$.

Elementary Analysis as $\text{C}_{25}\text{H}_{27}\text{ClN}_8\text{O}_8\text{S}_2 \cdot 3.7 \text{H}_2\text{O}$.

Calculated : C, 40.92; H, 4.73; N, 15.27; Cl, 4.83; S, 8.74 (%).

15 Found : C, 41.15; H, 4.46; N, 15.52; Cl, 4.57; S, 8.45 (%).

Example 140



20 $^1\text{H-NMR}$ (D_2O) δ : 1.31 (3H, d, $J = 7.2$ Hz), 1.52 (3H, d, $J = 6.9$ Hz), 3.06 (1H, d, $J = 18.1$ Hz), 3.50 (1H, d, $J = 18.1$ Hz), 4.20 (1H, q, $J = 6.9$ Hz), 4.52 (1H, q, $J = 7.2$ Hz), 5.03 (1H, d, $J = 14.4$ Hz), 5.14 (1H, d, $J = 5.1$ Hz), 5.29 (1H, d, $J = 14.4$ Hz), 5.75 (1H, d, $J = 5.1$ Hz), 8.00 (2H, d, $J = 7.2$ Hz), 8.63 (2H, d, $J = 7.2$ Hz).

IR (KBr) cm^{-1} : 3398, 1775, 1730, 1612, 1538, 1516, 1466, 1397, 1356, 1327, 1288, 1197, 1158, 1110, 1066, 1035.

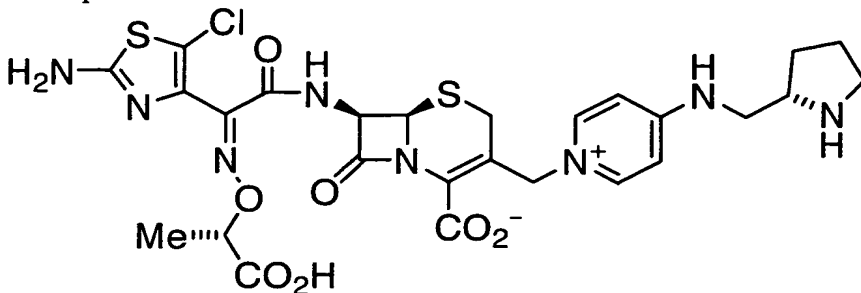
25 MS(ESI): 653 ($\text{M}+\text{H}$) $^+$.

Elementary Analysis as $C_{24}H_{25}ClN_8O_8S_2 \cdot 2.7 H_2O$.

Calculated : C, 41.08; H, 4.37; N, 15.97; Cl, 5.05; S, 9.14 (%).

Found : C, 41.13; H, 4.44; N, 15.94; Cl, 4.96; S, 8.94 (%).

5 Example 141



1H -NMR (D_2O) δ : 1.44 (3H, d, J = 7.5 Hz), 1.70-1.88 (1H, m), 1.98-2.20 (2H, m), 2.22-2.38 (1H, m), 3.17 (1H, d, J = 17.7 Hz), 3.30-3.42 (2H, m), 3.57 (1H, d, J = 17.7 Hz), 3.70 (2H, d, J = 6.3 Hz), 3.82-3.94 (1H, m), 4.66 (1H, q, J = 7.5 Hz), 4.87 (1H, d, J = 14.4 Hz), 5.10 (1H, d, J = 14.4 Hz), 5.23 (1H, d, J = 4.5 Hz), 5.85 (1H, d, J = 4.5 Hz), 6.93 (2H, d, J = 6.9 Hz), 8.05-8.30 (2H, m).

IR (KBr) cm^{-1} : 3398, 3065, 2983, 1774, 1650, 1602, 1556, 1447, 1394, 1360, 1287, 1218, 1168, 1096, 1064, 1034.

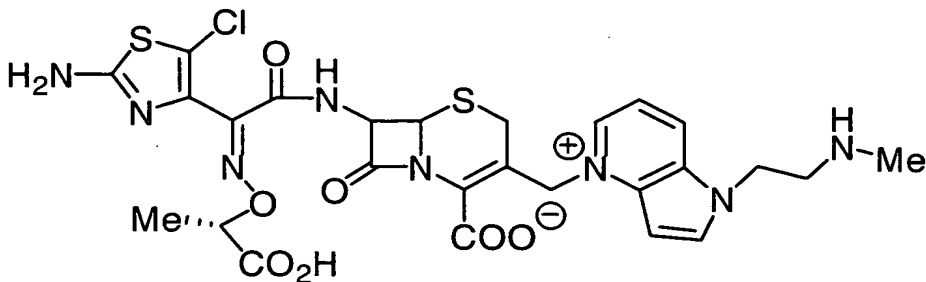
MS(FAB): 665 $^+$ (M+H $^+$).

15 Elementary Analysis as $C_{26}H_{29}ClN_8O_7S_2 \cdot 4.1 H_2O$.

Calculated : C, 42.26 ; H, 5.07 ; N, 15.16 ; Cl, 4.80 ; S, 8.68 (%).

Found : C, 42.29 ; H, 4.82 ; N, 15.26 ; Cl, 4.67 ; S, 8.53 (%).

Example 142



1H -NMR (D_2O) δ : 1.44(3H, d, J = 7.2 Hz), 2.73(3H, s), 3.17 and 3.38 (2H, ABq, J = 18.0 Hz), 3.63(2H, t, J = 6.0 Hz), 4.65(1H, q, J = 7.2 Hz), 4.80(2H, t, J = 6.0 Hz), 5.17(1H, d, J = 4.8 Hz), 5.56 and 5.69(2H, ABq, J = 15.0 Hz), 5.85(1H, d, J = 4.8 Hz), 7.09(1H, d, J = 3.3 Hz), 7.73(1H, dd, J = 6.3 and 8.4 Hz), 8.15(1H, d, J = 3.3 Hz), 8.62(1H, d, J = 8.4 Hz), 8.68(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1} : 3407, 2452, 1773, 1603, 1539, 1500, 1467, 1392, 1364, 1287, 1184, 1120, 1089, 1063, 1032.

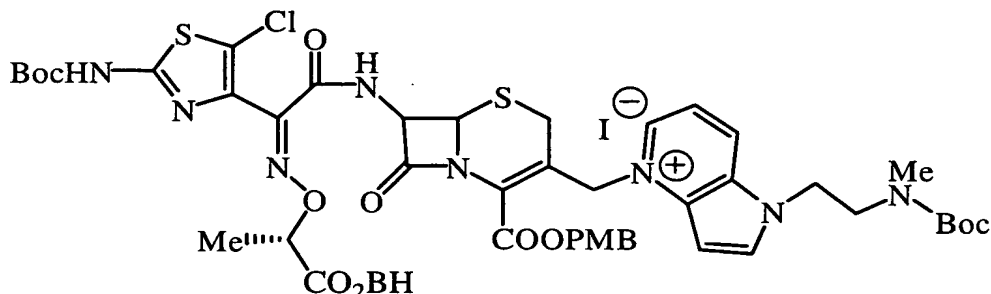
MS(FAB): 663⁺(M+H⁺).

Elementary Analysis as $\text{C}_{26}\text{H}_{27}\text{ClN}_8\text{O}_7\text{S}_2 \cdot 5.2 \text{H}_2\text{O}$.

5 Calculated : C, 41.26 ; H, 4.98 ; N, 14.81 ; Cl, 4.68 ; S, 8.47 (%).

Found : C, 41.41 ; H, 4.90 ; N, 14.55 ; Cl, 4.54 ; S, 8.46 (%).

quaternary salt ester :

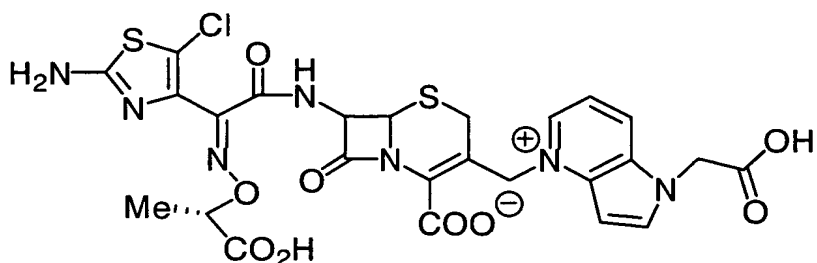


¹H-NMR (d_6 -DMSO) δ : 1.04(9H, brs), 1.43(3H, d, $J = 7.2$ Hz), 1.46(9H, s), 2.78(3H, brs), 3.21 and 3.40(2H, Abq, $J = 18.6$ Hz), 3.60(2H, m), 3.76(3H, s), 4.60(2H, t-like), 4.89(1H, q, $J = 7.2$ Hz), 5.20(1H, d, $J = 5.1$ Hz), 5.23 and 5.31(2H, Abq, $J = 11.7$ Hz), 5.71(2H, brs), 5.97(1H, dd, $J = 5.1$ and 8.7 Hz), 6.82(1H, s), 6.92(2H, d, $J = 8.7$ Hz), 7.01(1H, d, $J = 3.3$ Hz), 7.22-7.42(12H, m), 7.83(1H, brs), 8.30(1H, d, $J = 3.3$ Hz), 8.65(1H, brs), 8.84(1H, brs), 9.77(1H, d, $J = 8.7$ Hz), 12.1(brs).

15 IR (KBr) cm^{-1} : 3422, 3061, 3032, 2977, 2935, 1791, 1717, 1690, 1631, 1613, 1584, 1550, 1515, 1495, 1455, 1392, 1367, 1248, 1155, 1118, 1100, 1065, 1032, 1018.

MS(FAB): 1149⁺($\text{C}_{57}\text{H}_{62}\text{ClN}_8\text{O}_{12}\text{S}_2$).

20 Example 143



¹H-NMR (D_2O) δ : 1.43(3H, d, $J = 7.2$ Hz), 3.21 and 3.35 (2H, ABq, $J = 18.0$ Hz), 4.64(1H, q, $J = 7.2$ Hz), 5.01(2H, s), 5.17(1H, d, $J = 4.8$ Hz), 5.53 and 5.74(2H, ABq, $J = 15.0$ Hz), 5.89(1H, d, $J = 4.8$ Hz), 6.98(1H, d, $J = 3.3$ Hz), 7.67(1H, dd, $J = 6.3$ and 8.1 Hz), 8.04(1H, d, $J = 3.3$ Hz), 8.44(1H, d, $J = 8.1$ Hz), 8.62(1H, d, $J = 6.3$ Hz).

IR (KBr) cm^{-1} : 3415, 2989, 2527, 1778, 1725, 1672, 1630, 1537, 1500, 1467, 1373, 1328, 1229, 1162, 1129, 1063, 1035.

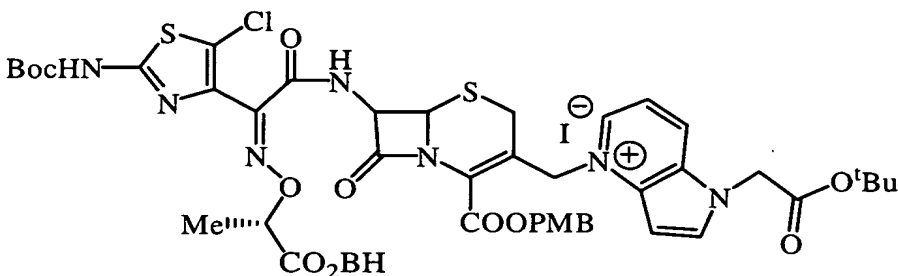
MS(ESI): 664⁺(M+H⁺).

Elementary Analysis as $\text{C}_{25}\text{H}_{22}\text{ClN}_7\text{O}_9\text{S}_2 \cdot 3.0 \text{ H}_2\text{O}$.

5 Calculated : C, 41.81 ; H, 3.93 ; N, 13.65 ; Cl, 4.94 ; S, 8.93 (%).

Found : C, 41.75 ; H, 3.89 ; N, 13.71 ; Cl, 5.08 ; S, 8.84 (%).

quaternary salt ester :



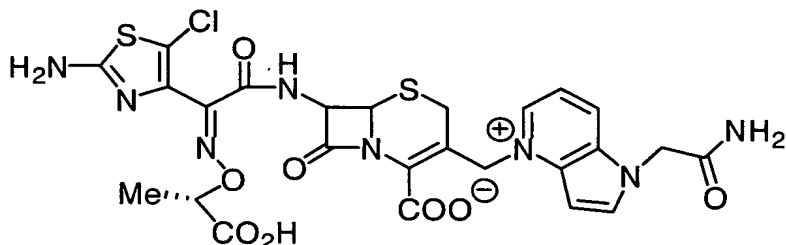
10 ¹H-NMR (d_6 -DMSO) δ : 1.42(3H, d, $J = 7.2$ Hz), 1.44(9H, s), 1.46(9H, s), 3.37(2H, brs), 3.75(3H, s), 4.89(1H, q, $J = 7.2$ Hz), 5.20(1H, d, $J = 5.1$ Hz), 5.21 and 5.29(2H, Abq, $J = 12.0$ Hz), 5.38(2H, brs), 5.72(2H, brs), 5.96(1H, dd, $J = 5.1$ and 8.7 Hz), 6.82(1H, s), 6.89(2H, d, $J = 8.7$ Hz), 7.00(1H, d, $J = 3.3$ Hz), 7.22-7.42(12H, m), 7.80(1H, dd, $J = 6.3$ and 8.4 Hz), 8.31(1H, d, $J = 3.3$ Hz), 8.62(1H, d, $J = 6.3$ Hz), 8.82(1H, d, $J = 8.4$ Hz),
15 9.76(1H, d, $J = 8.7$ Hz), 12.1(brs).

IR (KBr) cm^{-1} : 3422, 3061, 3031, 2979, 2935, 1790, 1738, 1631, 1613, 1585, 1550, 1515, 1498, 1466, 1455, 1392, 1369, 1329, 1247, 1155, 1128, 1100, 1064, 1032.

MS(FAB): 1106⁺($\text{C}_{55}\text{H}_{57}\text{ClN}_7\text{O}_{12}\text{S}_2^+$).

20

Example 144



¹H-NMR (D_2O) δ : 1.43(3H, d, $J = 6.9$ Hz), 3.20 and 3.37 (2H, ABq, $J = 17.7$ Hz), 4.64(1H, q, $J = 6.9$ Hz), 5.17(1H, d, $J = 4.8$ Hz), 5.27(2H, s), 5.56 and 5.73(2H, ABq, $J = 15.0$ Hz), 5.88(1H, d, $J = 4.8$ Hz), 7.06(1H, d, $J = 3.3$ Hz), 7.70(1H, dd, $J = 6.3$ and 8.1 Hz), 8.07(1H, d, $J = 3.3$ Hz), 8.51(1H, d, $J = 8.1$ Hz), 8.67(1H, d, $J = 6.3$ Hz).

25

IR (KBr) cm^{-1} : 3407, 3191, 2988, 1776, 1684, 1615, 1537, 1500, 1467, 1364, 1331, 1225, 1189, 1160, 1131, 1063, 1034.

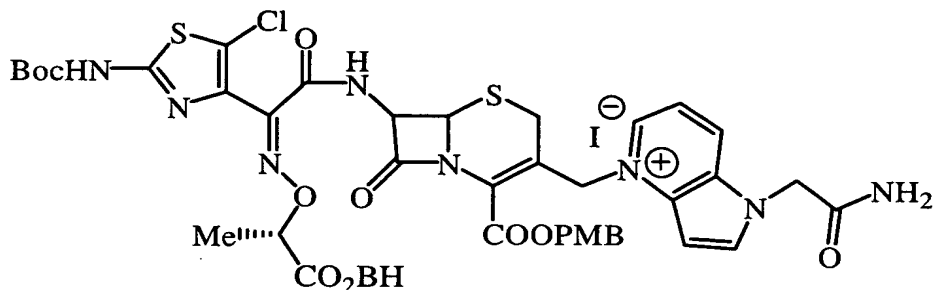
MS(ESI): 663⁺(M+H⁺).

Elementary Analysis as $\text{C}_{25}\text{H}_{23}\text{ClN}_8\text{O}_8\text{S}_2 \cdot 3.9 \text{ H}_2\text{O}$.

5 Calculated : C,40.95 ; H,4.23 ; N,15.28 ; Cl,4.83 ; S,8.74 (%).

Found : C,40.93 ; H,4.06 ; N,15.26 ; Cl,4.82 ; S,8.64 (%).

quaternary salt ester :

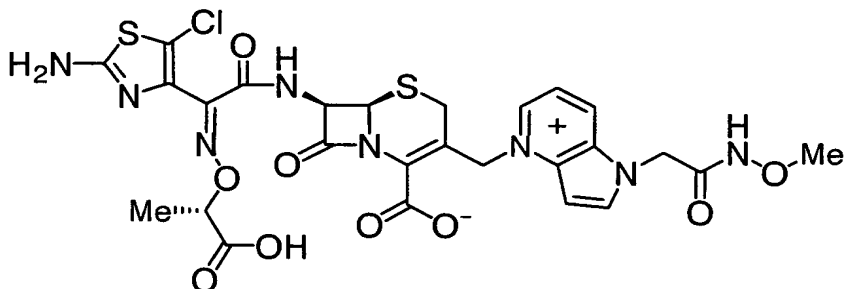


¹H-NMR (d_6 -DMSO) δ : 1.45(3H, d, J = 6.9 Hz), 1.46(9H, s), 3.39(2H, brs), 3.75(3H, s),
 10 4.89(1H, q, J = 6.9 Hz), 5.17(2H, brs), 5.20(1H, d, J = 4.8 Hz), 5.21 and 5.29(2H, Abq, J = 11.7 Hz), 5.70(2H, brs), 5.96(1H, dd, J = 4.8 and 8.7 Hz), 6.82(1H, s), 6.89(2H, d, J = 8.7 Hz), 6.96(1H, d, J = 3.3 Hz), 7.20-7.45(12H, m), 7.76(1H, dd, J = 6.0 and 8.7 Hz), 7.79(2H, brs), 8.29(1H, d, J = 3.3 Hz), 8.58(1H, d, J = 6.0 Hz), 8.73(1H, d, J = 8.7 Hz), 9.76(1H, d, J = 8.7 Hz), 12.1(brs).

15 IR (KBr) cm^{-1} : 3422, 3063, 2980, 2936, 1789, 1716, 1690, 1631, 1613, 1585, 1551, 1515, 1497, 1467, 1455, 1393, 1369, 1248, 1175, 1154, 1128, 1100, 1065, 1030, 1018.

MS(FAB): 1049⁺($\text{C}_{51}\text{H}_{50}\text{ClN}_8\text{O}_{11}\text{S}_2$ ⁺).

20 Example 145



¹H-NMR (D_2O) δ : 1.44(3H, d, J = 7.2 Hz), 3.20 and 3.37 (2H, ABq, J = 17.7 Hz), 3.73(3H, s), 4.65(1H, q, J = 7.2 Hz), 5.17(2H, s), 5.18(1H, d, J = 4.8 Hz), 5.56 and 5.73(2H, ABq, J = 15.0 Hz), 5.88(1H, d, J = 4.8 Hz), 7.06(1H, d, J = 3.3 Hz), 7.71(1H, dd, J = 6.3 and 8.1 Hz), 8.08(1H, d, J = 3.3 Hz), 8.53(1H, d,

$J = 8.1 \text{ Hz}$), 8.68(1H, d, $J = 6.3 \text{ Hz}$).

IR (KBr) cm^{-1} : 3422, 2985, 2938, 1778, 1678, 1615, 1537, 1501, 1466, 1442, 1365, 1330, 1225, 1188, 1159, 1129, 1065, 1034.

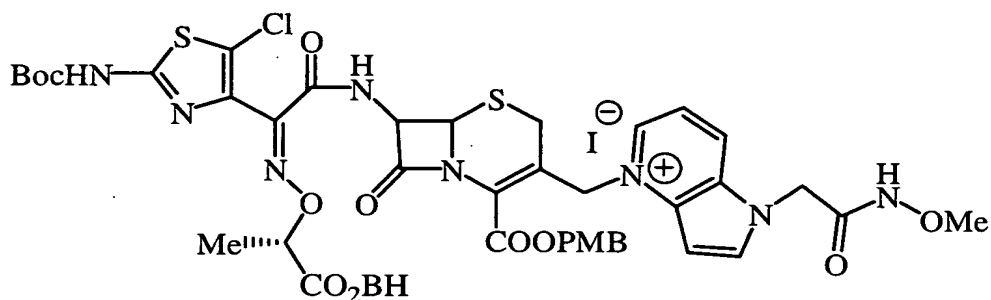
MS(FAB): 693⁺(M+H⁺).

5 Elementary Analysis as $\text{C}_{26}\text{H}_{25}\text{ClN}_8\text{O}_9\text{S}_2 \cdot 3.9 \text{ H}_2\text{O}$.

Calculated : C, 40.91 ; H, 4.33 ; N, 14.68 ; Cl, 4.64 ; S, 8.40 (%).

Found : C, 40.78 ; H, 4.14 ; N, 14.77 ; Cl, 4.67 ; S, 8.54 (%).

quaternary salt ester :



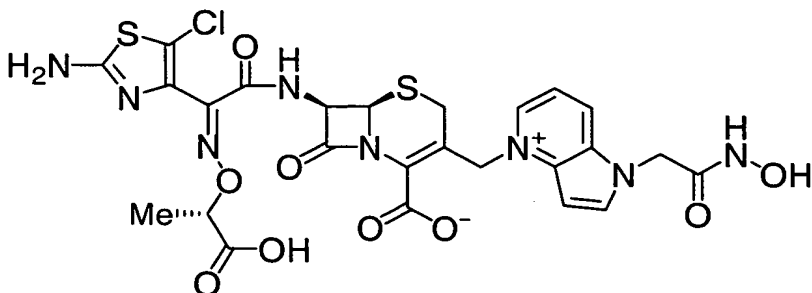
- 10 ¹H-NMR (d_6 -DMSO) δ : 1.44(3H, d, $J = 7.2 \text{ Hz}$), 1.46(9H, s), 3.39(2H, brs), 3.68(3H, s), 3.76(3H, s), 4.89(1H, q, $J = 7.2 \text{ Hz}$), 5.14(2H, brs), 5.20(1H, d, $J = 4.8 \text{ Hz}$), 5.21 and 5.28(2H, Abq, $J = 11.4 \text{ Hz}$), 5.71(2H, brs), 5.96(1H, dd, $J = 4.8$ and 8.7 Hz), 6.82(1H, s), 6.88(2H, d, $J = 8.7 \text{ Hz}$), 6.98(1H, d, $J = 3.0 \text{ Hz}$), 7.20-7.41(13H, m), 7.80(1H, dd, $J = 6.0$ and 8.1 Hz), 8.30(1H, d, $J = 3.0 \text{ Hz}$), 8.59(1H, d, $J = 6.0 \text{ Hz}$), 8.76(1H, d, $J = 8.1 \text{ Hz}$), 9.76(1H, d, $J = 8.7 \text{ Hz}$), 12.1(brs).
- 15

IR (KBr) cm^{-1} : 3428, 3101, 3063, 3031, 2980, 2937, 1789, 1717, 1632, 1613, 1585, 1550, 1515, 1497, 1466, 1391, 1369, 1326, 1247, 1175, 1155, 1127, 1100, 1064, 1032, 1018.

MS(FAB): 1079⁺($\text{C}_{52}\text{H}_{52}\text{ClN}_8\text{O}_{12}\text{S}_2$).

20

Example 146



¹H-NMR (D_2O) δ : 1.43(3H, d, $J = 7.2 \text{ Hz}$), 3.19 and 3.37 (2H, ABq, $J = 17.4 \text{ Hz}$), 4.65(1H, q, $J = 7.2 \text{ Hz}$), 5.17(1H, d, $J = 4.8 \text{ Hz}$), 5.19(2H, s), 5.56 and 5.72(2H, ABq, $J =$

15.0 Hz), 5.87(1H, d, J = 4.8 Hz), 7.06(1H, d, J = 3.3 Hz), 7.71(1H, dd, J = 6.0 and 8.1 Hz), 8.08(1H, d, J = 3.3 Hz), 8.52(1H, d, J = 8.1 Hz), 8.68(1H, d, J = 6.0 Hz).

IR (KBr) cm^{-1} : 3415, 2988, 1777, 1675, 1615, 1537, 1500, 1466, 1365, 1330, 1225, 1188, 1161, 1129, 1064, 1036.

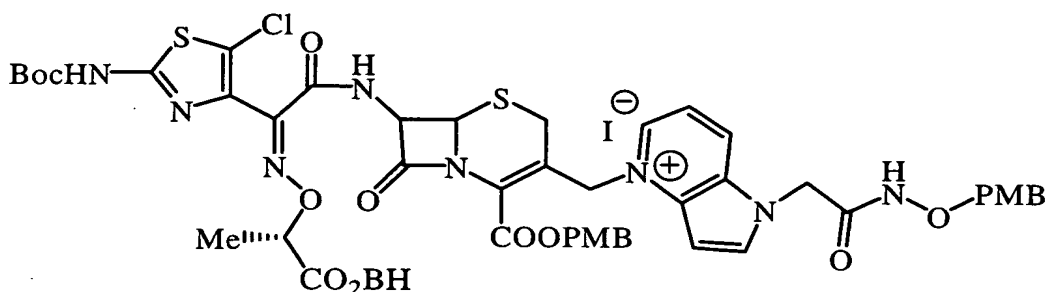
5 MS(FAB): 679⁺(M+H⁺).

Elementary Analysis as $\text{C}_{25}\text{H}_{23}\text{ClN}_8\text{O}_9\text{S}_2 \cdot 3.5 \text{H}_2\text{O}$.

Calculated : C, 40.46 ; H, 4.07 ; N, 15.10 ; Cl, 4.78 ; S, 8.64 (%).

Found : C, 40.45 ; H, 4.00 ; N, 15.08 ; Cl, 4.72 ; S, 8.57 (%).

quaternary salt ester :



10

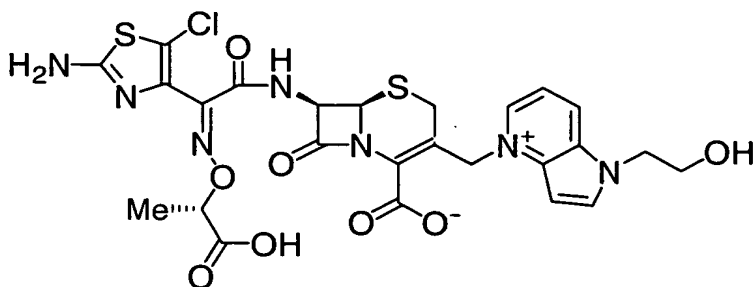
¹H-NMR (d_6 -DMSO) δ : 1.45(3H, d, J = 7.2 Hz), 1.46(9H, s), 3.40(2H, brs), 3.75(6H, s), 4.74(2H, brs), 4.89(1H, q, J = 7.2 Hz), 5.13(2H, brs), 5.20(1H, d, J = 5.1 Hz), 5.21 and 5.28(2H, Abq, J = 12.0 Hz), 5.71(2H, brs), 5.96(1H, dd, J = 5.1 and 8.7 Hz), 6.82(1H, s), 6.89(2H, d, J = 8.7 Hz), 6.99(1H, d, J = 3.3 Hz), 7.19-7.49(13H, m), 7.79(1H, dd, J = 6.3 and 8.7 Hz), 8.29(1H, d, J = 3.3 Hz), 8.61(1H, d, J = 6.3 Hz), 8.71(1H, d, J = 8.7 Hz), 9.76(1H, d, J = 8.7 Hz), 12.1(brs).

15

IR (KBr) cm^{-1} : 3421, 3063, 2978, 2936, 2836, 1790, 1716, 1631, 1612, 1585, 1549, 1514, 1497, 1465, 1369, 1325, 1248, 1176, 1154, 1125, 1100, 1064, 1030.

20 MS(FAB): 1185⁺($\text{C}_{59}\text{H}_{58}\text{ClN}_8\text{O}_{13}\text{S}_2^+$).

Example 147



¹H-NMR (D_2O) δ : 1.43(3H, d, J = 7.2 Hz), 3.18 and 3.34 (2H, ABq, J = 18.0 Hz), 3.97(2H, t, J = 4.8 Hz), 4.54(2H, t, J = 4.8 Hz), 4.64(1H, q, J = 7.2 Hz), 5.16(1H, d, J =

25

4.8 Hz), 5.53 and 5.71(2H, ABq, $J = 15.0$ Hz), 5.87(1H, d, $J = 4.8$ Hz), 7.00(1H, d, $J = 3.0$ Hz), 7.67(1H, dd, $J = 6.3$ and 8.1 Hz), 8.12(1H, d, $J = 3.0$ Hz), 8.59(1H, d, $J = 8.1$ Hz), 8.62(1H, d, $J = 6.3$ Hz).

IR (KBr) cm^{-1} : 3408, 2938, 1776, 1670, 1615, 1539, 1496, 1466, 1447, 1362,

5 1322, 1240, 1187, 1159, 1130, 1072, 1034.

MS(FAB): $650^+(\text{M}+\text{H}^+)$.

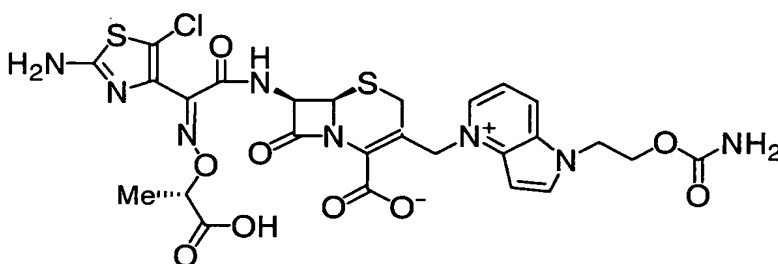
Elementary Analysis as $\text{C}_{25}\text{H}_{24}\text{ClN}_7\text{O}_8\text{S}_2 \cdot 4.1 \text{ H}_2\text{O}$.

Calculated : C, 41.48 ; H, 4.48 ; N, 13.54 ; Cl, 4.90 ; S, 8.86 (%).

Found : C, 41.48 ; H, 4.40 ; N, 13.59 ; Cl, 5.07 ; S, 8.88 (%).

10

Example 148



^1H -NMR (D_2O) δ : 1.44(3H, d, $J = 6.9$ Hz), 3.16 and 3.31 (2H, ABq, $J = 18.0$ Hz), 4.43(2H, t, $J = 4.5$ Hz), 4.65(1H, q, $J = 6.9$ Hz), 4.68(2H, t, $J = 4.5$ Hz), 5.17(1H, d, $J = 5.1$ Hz), 5.54 and 5.71(2H, ABq, $J = 15.0$ Hz), 5.87(1H, d, $J = 5.1$ Hz), 7.01(1H, d, $J = 3.0$ Hz), 7.69(1H, dd, $J = 6.3$ and 8.1 Hz), 8.12(1H, d, $J = 3.0$ Hz), 8.61(1H, d, $J = 8.1$ Hz), 8.63(1H, d, $J = 6.3$ Hz).

IR (KBr) cm^{-1} : 3415, 3193, 2987, 1777, 1718, 1673, 1614, 1537, 1497, 1466,

20 1447, 1364, 1328, 1225, 1188, 1135, 1080, 1034.

MS(FAB): $693^+(\text{M}+\text{H}^+)$.

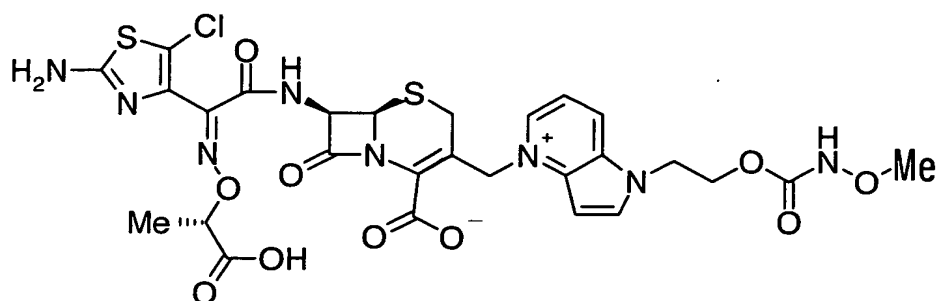
Elementary Analysis as $\text{C}_{26}\text{H}_{25}\text{ClN}_8\text{O}_9\text{S}_2 \cdot 3.0 \text{ H}_2\text{O}$.

Calculated : C, 41.80 ; H, 4.18 ; N, 15.00 ; Cl, 4.75 ; S, 8.58 (%).

Found : C, 41.68 ; H, 4.19 ; N, 14.79 ; Cl, 4.78 ; S, 8.91 (%).

25

Example 149



¹H-NMR (D₂O) δ: 1.43(3H, d, J = 7.2 Hz), 3.15 and 3.31(2H, ABq, J = 17.7 Hz), 3.47(3H, s), 4.54(2H, t, J = 4.8 Hz), 4.64(1H, q, J = 7.2 Hz), 4.72(2H, t, J = 4.8 Hz), 5.17(1H, d, J = 4.8 Hz), 5.54 and 5.71(2H, ABq, J = 15.0 Hz), 5.87(1H, d, J = 4.8 Hz), 7.02(1H, d, J = 3.3 Hz), 7.71(1H, dd, J = 6.3 and 8.4 Hz), 8.13(1H, d, J = 3.3 Hz), 8.62(1H, d, J = 8.4 Hz), 8.64(1H, d, J = 6.3 Hz).

IR (KBr) cm⁻¹: 3416, 2984, 2939, 1778, 1731, 1674, 1615, 1538, 1498, 1466, 1445, 1364, 1326, 1286, 1264, 1189, 1123, 1035.

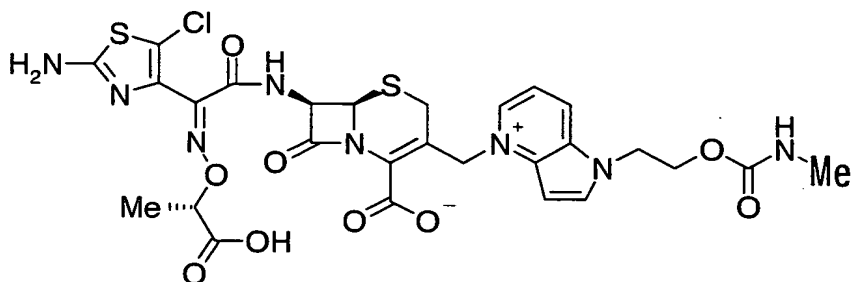
MS(FAB): 723⁺(M+H⁺).

10 Elementary Analysis as C₂₇H₂₇ClN₈O₁₀S₂ · 3.7 H₂O.

Calculated : C, 41.06 ; H, 4.39 ; N, 14.19 ; Cl, 4.49 ; S, 8.12 (%).

Found : C, 40.93 ; H, 4.29 ; N, 14.32 ; Cl, 4.63 ; S, 8.14 (%).

Example 150



15

¹H-NMR (D₂O) δ: 1.43(3H, d, J = 7.2 Hz), 2.45(3H, s), 3.15 and 3.31(2H, ABq, J = 17.7 Hz), 4.44(2H, brs), 4.64(1H, q, J = 7.2 Hz), 4.69(2H, brs), 5.17(1H, d, J = 4.8 Hz), 5.54 and 5.71(2H, ABq, J = 15.3 Hz), 5.87(1H, d, J = 4.8 Hz), 7.01(1H, d, J = 3.0 Hz), 7.69(1H, dd, J = 6.0 and 8.4 Hz), 8.11(1H, d, J = 3.0 Hz), 8.60(1H, d, J = 8.4 Hz), 8.64(1H, d, J = 6.0 Hz).

20

IR (KBr) cm⁻¹: 3401, 2984, 1779, 1710, 1676, 1617, 1538, 1498, 1466, 1364, 1326, 1265, 1187, 1135, 1097, 1033.

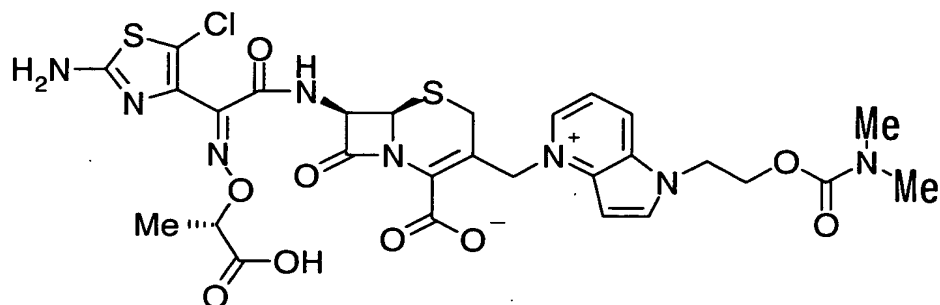
MS(FAB): 707⁺(M+H⁺).

Elementary Analysis as $C_{27}H_{27}ClN_8O_9S_2 \cdot 3.5 H_2O$.

Calculated : C,42.11 ; H,4.45 ; N,14.55 ; Cl,4.60 ; S,8.33 (%).

Found : C,42.18 ; H,4.37 ; N,14.52 ; Cl,4.63 ; S,8.12 (%).

5 Example 151



1H -NMR (D_2O) δ : 1.43(3H, d, J = 7.2 Hz), 2.66(3H, s), 2.70(3H, s), 3.14 and 3.30(2H, ABq, J = 17.7 Hz), 4.46(2H, t, J = 4.8 Hz), 4.64(1H, q, J = 7.2 Hz), 4.72(2H, t, J = 4.8 Hz), 5.17(1H, d, J = 5.1 Hz), 5.55 and 5.71(2H, ABq, J = 15.3 Hz), 5.87(1H, d, J = 5.1 Hz),
10 7.02(1H, d, J = 3.3 Hz), 7.70(1H, dd, J = 6.6 and 8.1 Hz), 8.15(1H, d, J = 3.3 Hz), 8.64(1H, d, J = 8.1 Hz), 8.65(1H, d, J = 6.6 Hz).

IR (KBr) cm^{-1} : 3422, 2938, 1779, 1690, 1617, 1538, 1497, 1466, 1363, 1325, 1287, 1190, 1135, 1098, 1066, 1034.

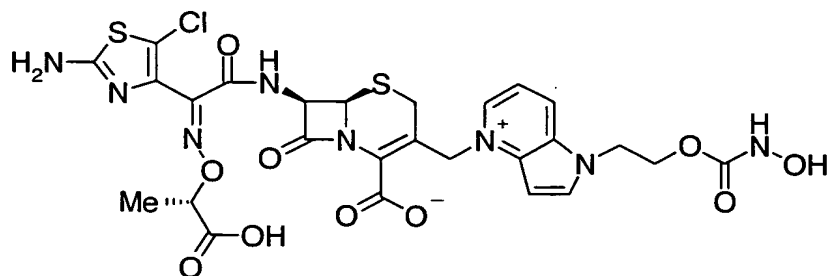
MS(FAB): 721 $^+(M+H^+)$.

15 Elementary Analysis as $C_{28}H_{29}ClN_8O_9S_2 \cdot 3.5 H_2O$.

Calculated : C,42.88 ; H,4.63 ; N,14.29 ; Cl,4.52 ; S,8.18 (%).

Found : C,42.81 ; H,4.62 ; N,14.23 ; Cl,4.50 ; S,8.38 (%).

Example 152



20 1H -NMR (D_2O) δ : 1.43(3H, d, J = 7.2 Hz), 3.17 and 3.32(2H, ABq, J = 17.7 Hz), 4.52(2H, t, J = 4.8 Hz), 4.65(1H, q, J = 7.2 Hz), 4.71(2H, t, J = 4.8 Hz), 5.17(1H, d, J = 4.8 Hz), 5.53 and 5.71(2H, ABq, J = 15.0 Hz), 5.87(1H, d, J = 4.8 Hz), 7.00(1H, d, J = 3.3 Hz), 7.70(1H, dd, J = 6.0 and 8.4 Hz), 8.11(1H, d, J = 3.3 Hz), 8.61(1H, d, J = 8.4 Hz), 8.63(1H, d, J = 6.0 Hz).

IR (KBr) cm^{-1} : 3307, 2938, 1777, 1728, 1673, 1613, 1537, 1498, 1466, 1364, 1326, 1285, 1188, 1122, 1034.

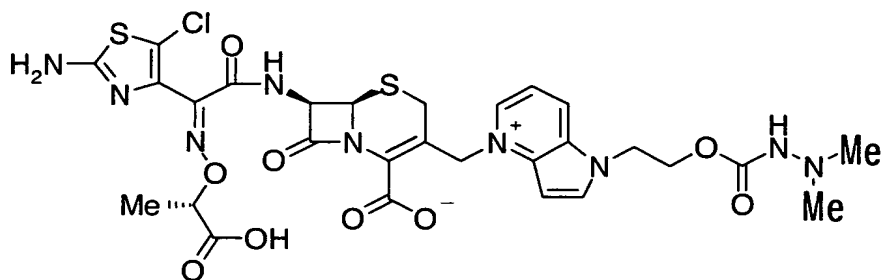
MS(FAB): 709⁺(M+H⁺).

Elementary Analysis as $\text{C}_{26}\text{H}_{25}\text{ClN}_8\text{O}_{10}\text{S}_2 \cdot 3.5 \text{ H}_2\text{O}$.

5 Calculated : C, 40.44 ; H, 4.18 ; N, 14.51 ; Cl, 4.59 ; S, 8.31 (%).

Found : C, 40.45 ; H, 4.15 ; N, 14.48 ; Cl, 4.70 ; S, 8.41 (%).

Example 153



10 ¹H-NMR (D₂O) δ : 1.44(3H, d, J = 7.2 Hz), 2.33(6H, s), 3.17 and 3.33(2H, ABq, J = 17.7 Hz), 4.48(2H, brs), 4.65(1H, q, J = 7.2 Hz), 4.69(2H, brs), 5.18(1H, d, J = 4.8 Hz), 5.54 and 5.71(2H, ABq, J = 14.7 Hz), 5.87(1H, d, J = 4.8 Hz), 7.03(1H, d, J = 3.3 Hz), 7.72(1H, dd, J = 6.0 and 8.7 Hz), 8.13(1H, d, J = 3.3 Hz), 8.60(1H, d, J = 8.7 Hz), 8.64(1H, d, J = 6.0 Hz).

15 IR (KBr) cm^{-1} : 3412, 2900, 2960, 1779, 1723, 1671, 1626, 1541, 1498, 1466, 1449, 1427, 1364, 1326, 1286, 1244, 1187, 1163, 1135, 1114, 1035.

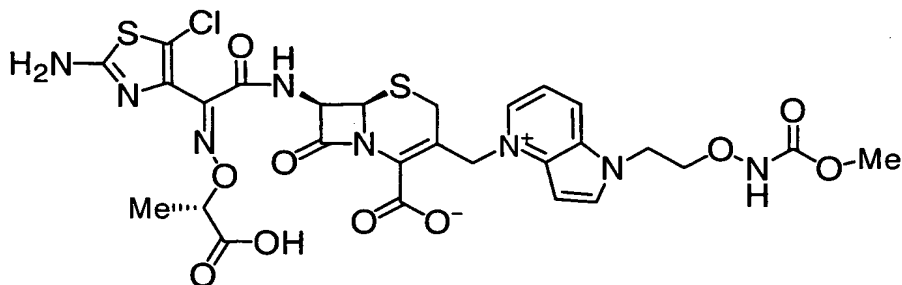
MS(FAB): 636⁺(M+H⁺).

Elementary Analysis as $\text{C}_{28}\text{H}_{30}\text{ClN}_9\text{O}_9\text{S}_2 \cdot 4.2 \text{ H}_2\text{O}$.

Calculated : C, 41.42 ; H, 4.77 ; N, 15.53 ; Cl, 4.37 ; S, 7.90 (%).

20 Found : C, 41.36 ; H, 4.55 ; N, 15.46 ; Cl, 4.36 ; S, 8.17 (%).

Example 154



¹H-NMR (D₂O) δ : 1.43(3H, d, J = 6.9 Hz), 3.17 and 3.33(2H, ABq, J = 17.7 Hz), 3.62(3H, s), 4.29(2H, t, J = 4.8 Hz), 4.64(1H, q, J = 6.9 Hz), 4.69(2H, t, J = 4.8 Hz),

5.17(1H, d, J = 4.5 Hz), 5.54 and 5.72(2H, ABq, J = 15.0 Hz), 5.87(1H, d, J = 4.5 Hz), 7.02(1H, d, J = 3.3 Hz), 7.68(1H, dd, J = 6.3 and 8.4 Hz), 8.18(1H, d, J = 3.3 Hz), 8.61(1H, d, J = 8.4 Hz), 8.63(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1} : 3415, 2988, 2953, 1778, 1674, 1616, 1538, 1498, 1466, 1363,

5 1321, 1285, 1190, 1132, 1062, 1035.

MS(FAB): 723⁺(M+H⁺).

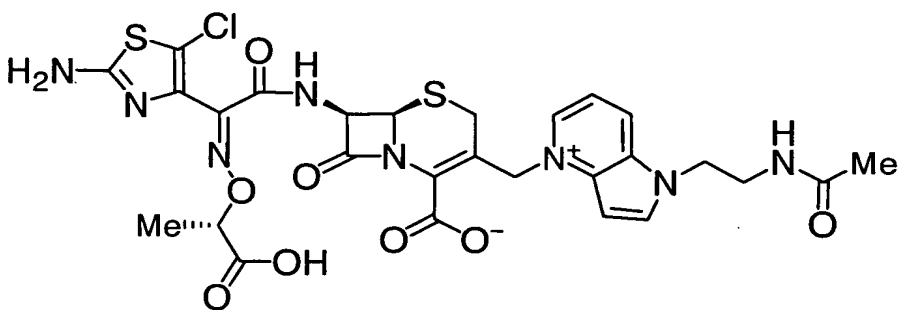
Elementary Analysis as $\text{C}_{27}\text{H}_{27}\text{ClN}_8\text{O}_{10}\text{S}_2 \cdot 4.1 \text{H}_2\text{O}$.

Calculated : C, 40.69 ; H, 4.45 ; N, 14.06 ; Cl, 4.45 ; S, 8.05 (%).

Found : C, 40.47 ; H, 4.28 ; N, 14.18 ; Cl, 4.88 ; S, 8.56 (%).

10

Example 155



¹H-NMR (D₂O) δ : 1.43(3H, d, J = 6.9 Hz), 1.74(3H, s), 3.18 and 3.33(2H, ABq, J = 17.7 Hz), 3.62(2H, t, J = 5.4 Hz), 4.53(2H, t, J = 5.4 Hz), 4.65(1H, q, J = 6.9 Hz), 5.18(1H, d, J = 4.8 Hz), 5.53 and 5.71(2H, ABq, J = 14.7 Hz), 5.87(1H, d, J = 4.8 Hz), 6.99(1H, d, J = 3.0 Hz), 7.69(1H, dd, J = 6.3 and 8.4 Hz), 8.07(1H, d, J = 3.0 Hz), 8.57(1H, d, J = 8.4 Hz), 8.62(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1} : 3400, 2938, 1777, 1629, 1540, 1497, 1467, 1450, 1368, 1323,

1288, 1240, 1189, 1159, 1134, 1095, 1035.

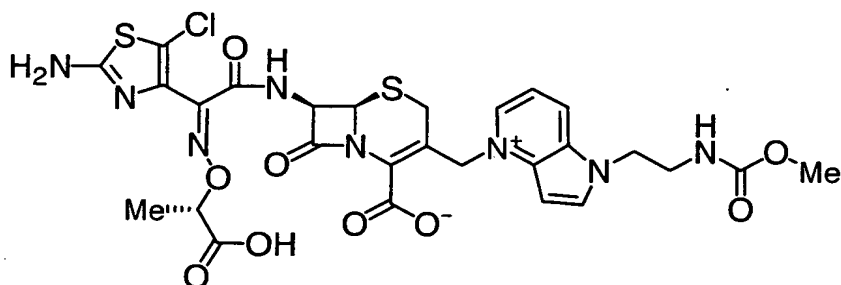
20 MS(FAB): 691⁺(M+H⁺).

Elementary Analysis as $\text{C}_{27}\text{H}_{27}\text{ClN}_8\text{O}_8\text{S}_2 \cdot 4.1 \text{H}_2\text{O}$.

Calculated : C, 41.51 ; H, 4.77 ; N, 14.34 ; Cl, 4.54 ; S, 8.21 (%).

Found : C, 41.33 ; H, 4.56 ; N, 14.36 ; Cl, 4.88 ; S, 8.39 (%).

25 Example 156



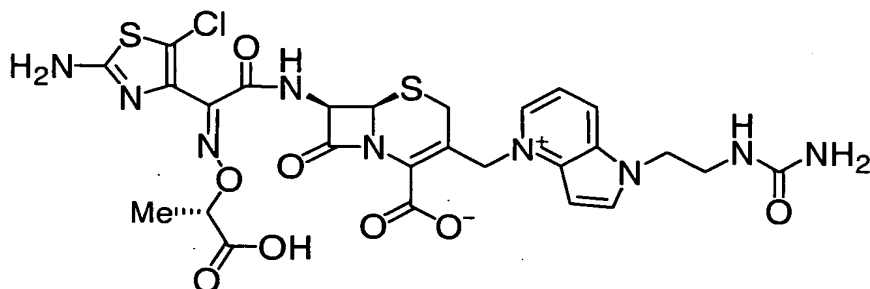
¹H-NMR (D₂O) δ : 1.43(3H, d, J = 7.5 Hz), 3.15 and 3.32(2H, ABq, J = 17.7 Hz), 3.91(3H, s), 3.57(2H, brs), 4.51(2H, m), 4.65(1H, q, J = 7.5 Hz), 5.17(1H, d, J = 4.8 Hz), 5.55 and 5.70(2H, ABq, J = 14.7 Hz), 5.87(1H, d, J = 4.8 Hz), 7.00(1H, d, J = 3.3 Hz), 7.69(1H, dd, J = 6.0 and 8.1 Hz), 8.09(1H, d, J = 3.3 Hz), 8.59(1H, d, J = 8.1 Hz), 8.64(1H, d, J = 6.0 Hz).

IR (KBr) cm⁻¹: 3410, 2987, 2940, 1777, 1677, 1626, 1537, 1499, 1466, 1365, 1322, 1271, 1191, 1157, 1132, 1096, 1035.

MS(FAB): 07⁺(M+H⁺).

10 HR-MS(FAB): calcd for C₂₇H₂₈ClN₈O₉S₂ 707.1109 found 707.1106.

Example 157



¹H-NMR (D₂O) δ : 1.44(3H, d, J = 6.9 Hz), 3.18 and 3.33(2H, ABq, J = 17.7 Hz), 3.54(2H, t, J = 4.5 Hz), 4.49(2H, t, J = 4.5 Hz), 4.65(1H, q, J = 6.9 Hz), 5.17(1H, d, J = 5.1 Hz), 5.52 and 5.70(2H, ABq, J = 15.0 Hz), 5.87(1H, d, J = 5.1 Hz), 6.98(1H, d, J = 3.3 Hz), 7.67(1H, dd, J = 6.3 and 8.1 Hz), 8.07(1H, d, J = 3.3 Hz), 8.55(1H, d, J = 8.1 Hz), 8.60(1H, d, J = 6.3 Hz).

IR (KBr) cm⁻¹: 3375, 1773, 1660, 1609, 1543, 1497, 1466, 1451, 1362, 1288,

20 1240, 1188, 1159, 1133, 1098, 1035.

MS(FAB): 692⁺(M+H⁺).

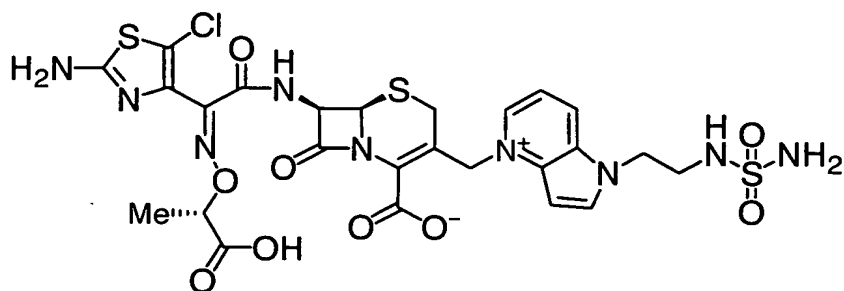
HR-MS(FAB): calcd for C₂₆H₂₇ClN₉O₈S₂ 692.1113 found 692.1100.

Elementary Analysis as C₂₆H₂₆ClN₉O₈S₂ · 4.3 H₂O.

Calculated : C, 40.58 ; H, 4.53 ; N, 16.38 ; Cl, 4.61 ; S, 8.33 (%).

25 Found : C, 40.46 ; H, 4.38 ; N, 16.84 ; Cl, 5.26 ; S, 7.73 (%).

Example 158



$^1\text{H-NMR}$ (D_2O) δ : 1.43(3H, d, $J = 7.2$ Hz), 3.14 and 3.31(2H, ABq, $J = 17.7$ Hz),
 5 3.53(2H, t-like), 4.57(2H, t-like), 4.64(1H, q, $J = 7.2$ Hz), 5.17(1H, d, $J = 4.8$ Hz), 5.54
 and 5.70(2H, ABq, $J = 15.0$ Hz), 5.87(1H, d, $J = 4.8$ Hz), 7.00(1H, d, $J = 3.3$ Hz), 7.68(1H,
 dd, $J = 6.3$ and 8.4 Hz), 8.13(1H, d, $J = 3.3$ Hz), 8.62(1H, d, $J = 8.4$ Hz), 8.62(1H, d, $J =$
 6.3 Hz).

IR (KBr) cm^{-1} : 3316, 1775, 1671, 1611, 1538, 1497, 1467, 1448, 1363, 1326,

1241, 1157, 1134, 1097, 1035.

MS(FAB): 728 $^+$ ($\text{M}+\text{H}^+$).

Elementary Analysis as $\text{C}_{25}\text{H}_{26}\text{ClN}_9\text{O}_9\text{S}_3 \cdot 3.6 \text{ H}_2\text{O}$.

Calculated : C, 37.86 ; H, 4.22 ; N, 15.90 ; Cl, 4.47 ; S, 12.13 (%).

Found : C, 37.88 ; H, 4.10 ; N, 15.92 ; Cl, 4.37 ; S, 12.00 (%).

15 IR (KBr) cm^{-1} : 3316, 1775, 1671, 1611, 1538, 1497, 1467, 1448, 1363, 1326,

1241, 1157, 1134, 1097, 1035.

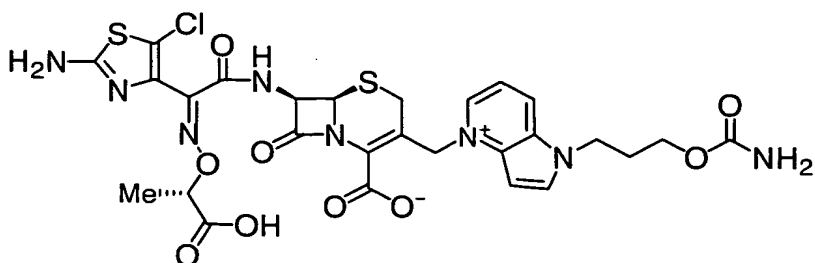
MS(FAB): 728 $^+$ ($\text{M}+\text{H}^+$).

Elementary Analysis as $\text{C}_{25}\text{H}_{26}\text{ClN}_9\text{O}_9\text{S}_3 \cdot 3.6 \text{ H}_2\text{O}$.

Calculated : C, 37.86 ; H, 4.22 ; N, 15.90 ; Cl, 4.47 ; S, 12.13 (%).

20 Found : C, 37.88 ; H, 4.10 ; N, 15.92 ; Cl, 4.37 ; S, 12.00 (%).

Example 159



$^1\text{H-NMR}$ (D_2O) δ : 1.44(3H, d, $J = 6.9$ Hz), 2.25(2H, m), 3.17 and 3.33(2H, ABq, $J =$
 25 17.7 Hz), 3.95(2H, t, $J = 5.7$ Hz), 4.54(2H, t, $J = 6.3$ Hz), 4.65(1H, q, $J = 6.9$ Hz), 5.17(1H,

d, J = 5.1 Hz), 5.53 and 5.70(2H, ABq, J = 15.0 Hz), 5.87(1H, d, J = 5.1 Hz), 7.00(1H, d, J = 3.3 Hz), 7.67(1H, dd, J = 6.3 and 8.4 Hz), 8.12(1H, d, J = 3.3 Hz), 8.59(1H, d, J = 8.4 Hz), 8.61(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1} : 3402, 3193, 2985, 1777, 1710, 1673, 1612, 1539, 1497, 1457,

5 1362, 1331, 1239, 1189, 1132, 1103, 1078, 1036.

MS(FAB): 707⁺(M+H⁺).

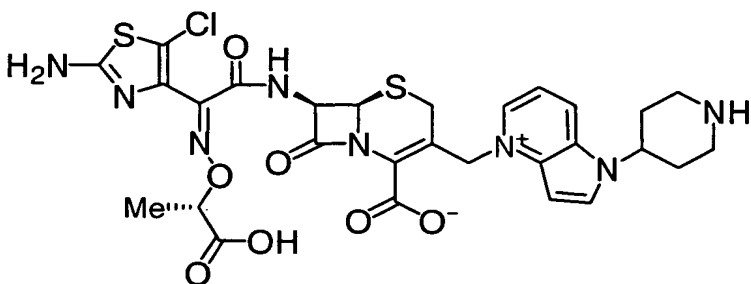
Elementary Analysis as $\text{C}_{27}\text{H}_{27}\text{ClN}_8\text{O}_9\text{S}_2 \cdot 3.4 \text{ H}_2\text{O}$.

Calculated : C, 42.20 ; H, 4.43 ; N, 14.58 ; Cl, 4.61 ; S, 8.35 (%).

Found : C, 42.19 ; H, 4.34 ; N, 14.60 ; Cl, 4.54 ; S, 8.23 (%).

10

Example 160



¹H-NMR (D₂O) δ : 1.43(3H, d, J = 7.2 Hz), 2.26-2.42(4H, m), 3.15 and 3.34(2H, ABq, J = 17.7 Hz), 3.28(2H, dt, J = 3.0 and 12.6 Hz), 3.64(2H, d, J = 12.6 Hz), 4.65(1H, q, J = 7.2 Hz), 4.91-5.00(1H, m), 5.16(1H, d, J = 4.8 Hz), 5.55 and 5.69(2H, ABq, J = 15.0 Hz), 5.85(1H, d, J = 4.8 Hz), 7.06(1H, d, J = 3.6 Hz), 7.69(1H, dd, J = 6.3 and 8.4 Hz), 8.23(1H, d, J = 3.6 Hz), 8.64(1H, d, J = 8.4 Hz), 8.65(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1} : 3397, 2528, 1773, 1599, 1539, 1494, 1461, 1396, 1360, 1315, 1285, 1185, 1128, 1068, 1032.

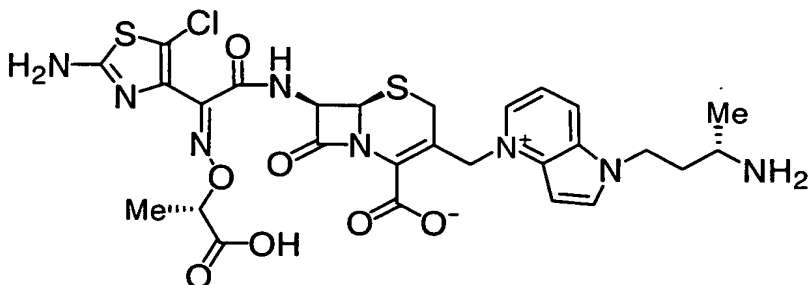
20 MS(FAB): 689⁺(M+H⁺).

Elementary Analysis as $\text{C}_{28}\text{H}_{29}\text{ClN}_8\text{O}_7\text{S}_2 \cdot 6.5 \text{ H}_2\text{O}$.

Calculated : C, 41.71 ; H, 5.25 ; N, 13.90 ; Cl, 4.40 ; S, 7.95 (%).

Found : C, 41.69 ; H, 5.13 ; N, 13.96 ; Cl, 4.35 ; S, 7.78 (%).

25 Example 161



¹H-NMR (D₂O) δ : 1.36(3H, d, J = 6.9 Hz), 1.43(3H, d, J = 7.2 Hz), 2.10-2.37(2H, m), 3.16 and 3.36(2H, ABq, J = 17.7 Hz), 3.31-3.42(1H, m), 4.52(2H, t-like), 4.65(1H, q, J = 7.2 Hz), 5.17(1H, d, J = 4.8 Hz), 5.54 and 5.69(2H, ABq, J = 15.0 Hz), 5.85(1H, d, J = 4.8 Hz), 7.02(1H, d, J = 3.3 Hz), 7.69(1H, dd, J = 6.0 and 8.7 Hz), 8.14(1H, d, J = 3.3 Hz), 8.59(1H, d, J = 8.7 Hz), 8.63(1H, d, J = 6.0 Hz).

IR (KBr) cm⁻¹: 3388, 2981, 1775, 1591, 1539, 1499, 1458, 1393, 1363, 1286, 1221, 1186, 1160, 1114, 1062, 1033.

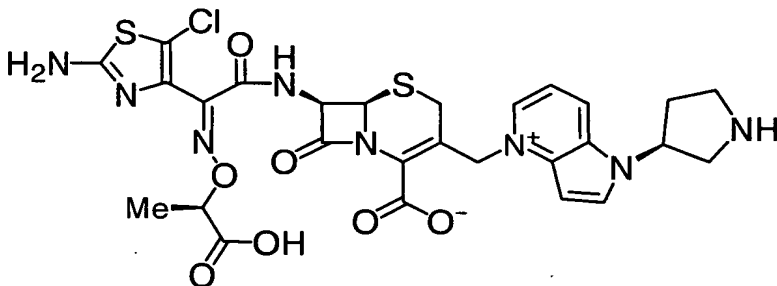
MS(FAB): 677⁺(M+H⁺).

10 Elementary Analysis as C₂₇H₂₉ClN₈O₇S₂ · 5.4 H₂O.

Calculated : C, 41.87 ; H, 5.18 ; N, 14.47 ; Cl, 4.58 ; S, 8.28 (%).

Found : C, 41.81 ; H, 4.96 ; N, 14.40 ; Cl, 4.69 ; S, 8.30 (%).

Example 162



¹H-NMR (D₂O) δ : 1.42(3H, d, J = 6.9 Hz), 2.30(1H, m), 2.54(1H, m), 3.19 and 3.33(2H, ABq, J = 18.0 Hz), 3.42-3.59(2H, m), 3.72-3.78(1H, m), 3.88-3.94(1H, m), 4.63(1H, q, J = 6.9 Hz), 5.18(1H, d, J = 4.8 Hz), 5.36(1H, m), 5.53 and 5.72(2H, ABq, J = 15.3 Hz), 5.82(1H, d, J = 4.8 Hz), 7.00(1H, d, J = 3.6 Hz), 7.69(1H, dd, J = 6.0 and 8.4 Hz), 8.08(1H, d, J = 3.6 Hz), 8.62(1H, d, J = 6.0 Hz), 8.63(1H, d, J = 8.4 Hz).

IR (KBr) cm⁻¹: 3387, 1770, 1667, 1605, 1543, 1495, 1461, 1399, 1359, 1321, 1285, 1202, 1149, 1131, 1081, 1058, 1029.

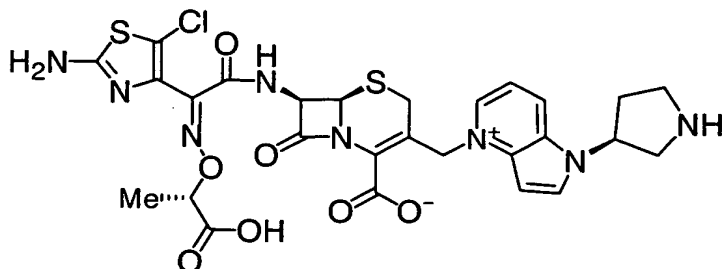
MS(ESI): 675⁺(M+H⁺).

Elementary Analysis as C₂₇H₂₇ClN₈O₇S₂ · 6.0 H₂O · 0.2(C₃H₇OH).

25 Calculated : C, 41.68 ; H, 5.15 ; N, 14.09 ; Cl, 4.46 ; S, 8.06 (%).

Found : C,41.53 ; H,5.05 ; N,14.16 ; Cl,4.35 ; S,7.82 (%).

Example 163



- 5 $^1\text{H-NMR}$ (D_2O) δ : 1.44(3H, d, $J = 7.2$ Hz), 2.30(1H, m), 2.53(1H, m), 3.19 and 3.33(2H, ABq, $J = 17.7$ Hz), 3.42-3.59(2H, m), 3.72-3.78(1H, m), 3.88-3.94 (1H, m), 4.66(1H, q, $J = 7.2$ Hz), 5.18(1H, d, $J = 5.1$ Hz), 5.38(1H, m), 5.52 and 5.71(2H, ABq, $J = 15.0$ Hz), 5.87(1H, d, $J = 5.1$ Hz), 7.00(1H, d, $J = 3.6$ Hz), 7.69(1H, dd, $J = 6.3$ and 8.4 Hz), 8.08(1H, d, $J = 3.6$ Hz), 8.62 (1H, d, $J = 6.3$ Hz), 8.64(1H, d, $J = 8.4$ Hz).

IR (KBr) cm^{-1} : 3406, 2978, 1772, 1601, 1541, 1497, 1461, 1395, 1364, 1313, 1287, 1222, 1186, 1161, 1132, 1094, 1065, 1034.

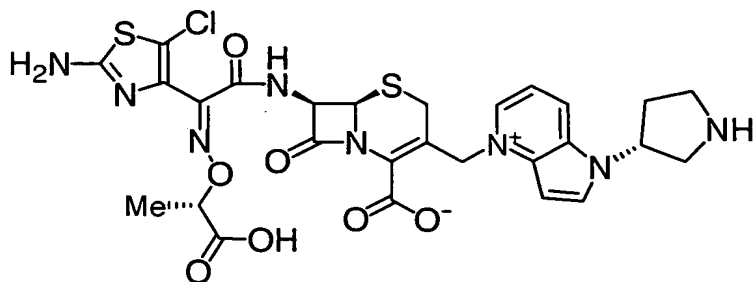
MS(ESI): 675 $^+$ ($\text{M}+\text{H}^+$).

Elementary Analysis as $\text{C}_{27}\text{H}_{27}\text{ClN}_8\text{O}_7\text{S}_2 \cdot 3.2 \text{H}_2\text{O} \cdot 0.45(\text{C}_3\text{H}_7\text{OH})$.

- 15 Calculated : C,44.81 ; H,4.91 ; N,14.75 ; Cl,4.67 ; S,8.44 (%).

Found : C,44.79 ; H,4.97 ; N,14.64 ; Cl,4.61 ; S,8.28 (%).

Example 164



- 20 $^1\text{H-NMR}$ (D_2O) δ : 1.44(3H, d, $J = 7.2$ Hz), 2.30(1H, m), 2.54(1H, m), 3.19 and 3.33(2H, ABq, $J = 18.0$ Hz), 3.42-3.59(2H, m), 3.72-3.77(1H, m), 3.88-3.94 (1H, m), 4.65(1H, q, $J = 7.2$ Hz), 5.18(1H, d, $J = 4.8$ Hz), 5.38(1H, m), 5.52 and 5.72(2H, ABq, $J = 14.7$ Hz), 5.88(1H, d, $J = 4.8$ Hz), 7.00(1H, d, $J = 3.3$ Hz), 7.69(1H, dd, $J = 6.0$ and 8.4 Hz), 8.08(1H, d, $J = 3.3$ Hz), 8.62(1H, d, $J = 6.0$ Hz), 8.65(1H, d, $J = 8.4$ Hz).

IR (KBr) cm^{-1} : 3397, 2982, 1773, 1602, 1540, 1497, 1462, 1395, 1364, 1316, 1287, 1186, 1132, 1092, 1064, 1034.

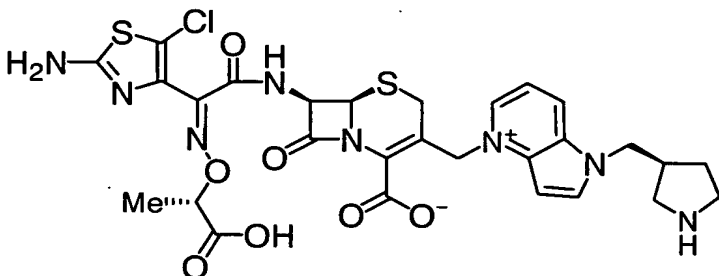
MS(ESI): 675⁺(M+H⁺).

Elementary Analysis as $\text{C}_{27}\text{H}_{27}\text{ClN}_8\text{O}_7\text{S}_2 \cdot 5.0 \text{ H}_2\text{O} \cdot 0.1(\text{C}_3\text{H}_7\text{OH})$.

5 Calculated : C, 42.52 ; H, 4.94 ; N, 14.53 ; Cl, 4.60 ; S, 8.32 (%).

Found : C, 42.54 ; H, 4.95 ; N, 14.29 ; Cl, 5.01 ; S, 8.09 (%).

Example 165



10 ¹H-NMR (D_2O) δ : 1.43(3H, d, J = 6.9 Hz), 1.76-1.89(1H, m), 2.08-2.18(1H, m), 2.98-3.52(5H, m), 3.18 and 3.37(2H, ABq, J = 18.3 Hz), 4.55(2H, d, J = 6.3 Hz), 4.65(1H, q, J = 6.9 Hz), 5.18(1H, d, J = 4.8 Hz), 5.55 and 5.70(2H, ABq, J = 15.0 Hz), 5.86(1H, d, J = 4.8 Hz), 7.04(1H, d, J = 3.3 Hz), 7.70(1H, dd, J = 6.3 and 8.1 Hz), 8.15(1H, d, J = 3.3 Hz), 8.63(1H, d, J = 8.1 Hz), 8.65(1H, d, J = 6.3 Hz).

15 IR (KBr) cm^{-1} : 3397, 2982, 1774, 1602, 1539, 1499, 1454, 1391, 1363, 1319, 1286, 1185, 1158, 1129, 1092, 1064, 1033.

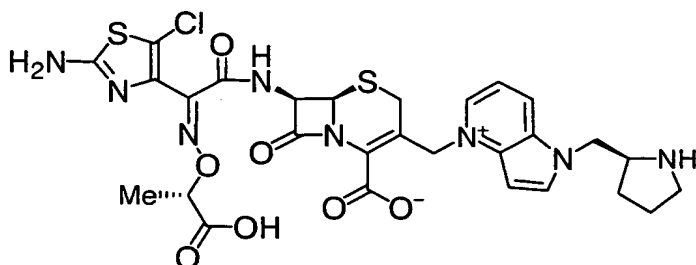
MS(FAB): 689⁺(M+H⁺).

Elementary Analysis as $\text{C}_{28}\text{H}_{29}\text{ClN}_8\text{O}_7\text{S}_2 \cdot 4.9 \text{ H}_2\text{O}$.

Calculated : C, 43.26 ; H, 5.03 ; N, 14.41 ; Cl, 4.56 ; S, 8.25 (%).

20 Found : C, 43.23 ; H, 5.01 ; N, 14.42 ; Cl, 4.47 ; S, 8.14 (%).

Example 166



25 ¹H-NMR (D_2O) δ : 1.43(3H, d, J = 6.9 Hz), 1.81-1.94(1H, m), 2.02-2.34(3H, m), 3.18 and 3.39(2H, ABq, J = 17.7 Hz), 3.26-3.49(2H, m), 4.09-4.19(1H, m), 4.65(1H, q, J = 6.9 Hz),

4.75(2H, brs), 5.18(1H, d, $J = 4.8$ Hz), 5.57 and 5.71(2H, ABq, $J = 15.3$ Hz), 5.86(1H, d, $J = 4.8$ Hz), 7.10(1H, d, $J = 3.0$ Hz), 7.74(1H, dd, $J = 6.3$ and 8.4 Hz), 8.17(1H, d, $J = 3.0$ Hz), 8.66(1H, d, $J = 8.4$ Hz), 8.69(1H, d, $J = 6.3$ Hz).

IR (KBr) cm^{-1} : 3396, 2982, 1775, 1602, 1540, 1501, 1465, 1391, 1364, 1287,

1186, 1158, 1131, 1092, 1064, 1033.

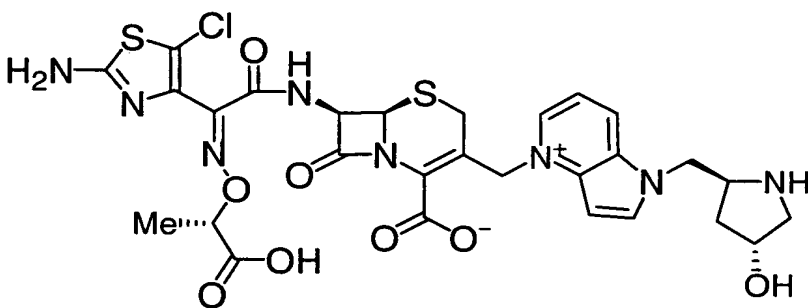
MS(FAB): 689⁺(M+H⁺).

Elementary Analysis as $\text{C}_{28}\text{H}_{29}\text{ClN}_8\text{O}_7\text{S}_2 \cdot 4.9 \text{ H}_2\text{O}$.

Calculated : C, 43.26 ; H, 5.03 ; N, 14.41 ; Cl, 4.56 ; S, 8.25 (%).

Found : C, 43.54 ; H, 5.01 ; N, 14.32 ; Cl, 4.40 ; S, 7.96 (%).

Example 167



¹H-NMR (D_2O) δ : 1.44(3H, d, $J = 7.2$ Hz), 2.02-2.31(2H, m), 3.18 and 3.40(2H, ABq, $J = 17.7$ Hz), 3.30(1H, d, $J = 12.9$ Hz), 3.65(1H, dd, $J = 4.8$ and 12.9 Hz), 4.37-4.50(1H, m), 4.66(1H, q, $J = 7.2$ Hz), 4.63-4.74(1H, m), 4.86(2H, m), 5.19(1H, d, $J = 5.1$ Hz), 5.58 and 5.71(2H, ABq, $J = 15.0$ Hz), 5.86(1H, d, $J = 5.1$ Hz), 7.12(1H, d, $J = 3.3$ Hz), 7.75(1H, dd, $J = 6.0$ and 8.4 Hz), 8.19(1H, d, $J = 3.3$ Hz), 8.67(1H, d, $J = 8.4$ Hz), 8.69(1H, d, $J = 6.0$ Hz).

IR (KBr) cm^{-1} : 3395, 2984, 1774, 1603, 1539, 1502, 1465, 1392, 1364, 1322, 1287, 1221,

1186, 1132, 1091, 1066, 1034.

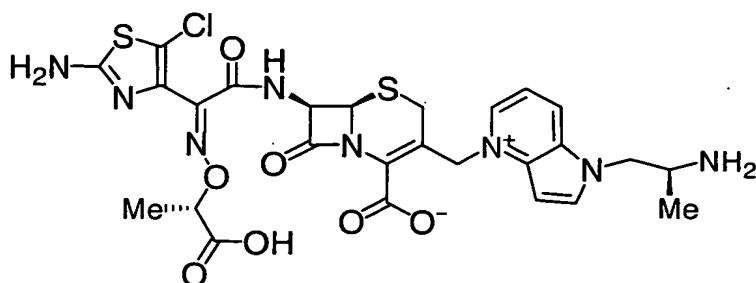
MS(FAB): 705⁺(M+H⁺).

Elementary Analysis as $\text{C}_{28}\text{H}_{29}\text{ClN}_8\text{O}_8\text{S}_2 \cdot 4.5 \text{ H}_2\text{O}$.

Calculated : C, 42.77 ; H, 4.87 ; N, 14.25 ; Cl, 4.51 ; S, 8.16 (%).

Found : C, 42.69 ; H, 4.51 ; N, 14.46 ; Cl, 4.36 ; S, 8.04 (%).

Example 168



$^1\text{H-NMR}$ (D_2O) δ : 1.39(3H, d, $J = 6.6$ Hz), 1.43(3H, d, $J = 6.9$ Hz), 3.18 and 3.38(2H, ABq, $J = 17.7$ Hz), 3.99(1H, q-like), 4.65(1H, q, $J = 6.9$ Hz), 4.66(2H, t-like), 5.18(1H, d, $J = 4.8$ Hz), 5.57 and 5.71(2H, ABq, $J = 15.0$ Hz), 5.86(1H, d, $J = 4.8$ Hz), 7.11(1H, d, $J = 3.0$ Hz), 7.74(1H, dd, $J = 6.3$ and 8.4 Hz), 8.14(1H, d, $J = 3.0$ Hz), 8.64(1H, d, $J = 8.4$ Hz), 8.69(1H, d, $J = 6.3$ Hz).

IR (KBr) cm^{-1} : 3397, 2983, 1773, 1597, 1539, 1502, 1466, 1395, 1364, 1325, 1289, 1181, 1112, 1063, 1033.

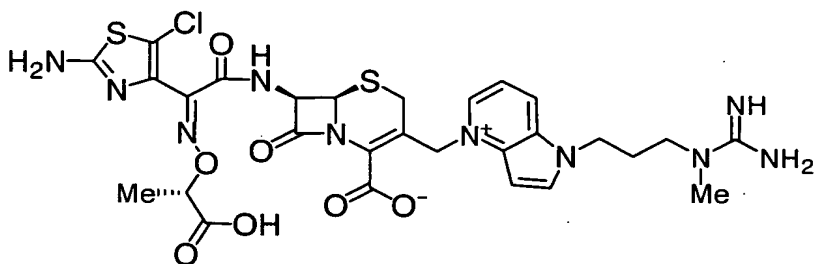
MS(FAB): 663 $^+$ ($\text{M}+\text{H}^+$).

10 Elementary Analysis as $\text{C}_{26}\text{H}_{27}\text{ClN}_8\text{O}_7\text{S}_2 \cdot 4.7 \text{ H}_2\text{O}$.

Calculated : C, 41.76 ; H, 4.91 ; N, 14.98 ; Cl, 4.74 ; S, 8.58 (%).

Found : C, 41.81 ; H, 4.80 ; N, 14.92 ; Cl, 4.70 ; S, 8.59 (%).

Example 169



$^1\text{H-NMR}$ (D_2O) δ : 1.43(3H, d, $J = 7.2$ Hz), 2.31(2H, quintet, $J = 7.2$ Hz), 2.91(3H, s), 3.17 and 3.37(2H, ABq, $J = 17.7$ Hz), 3.38(2H, t, $J = 7.2$ Hz), 4.48(2H, t, $J = 7.2$ Hz), 4.65(1H, q, $J = 7.2$ Hz), 5.18(1H, d, $J = 4.8$ Hz), 5.56 and 5.69(2H, ABq, $J = 15.0$ Hz), 5.85(1H, d, $J = 4.8$ Hz), 7.05(1H, d, $J = 3.3$ Hz), 7.69(1H, dd, $J = 6.0$ and 8.7 Hz), 8.14(1H, d, $J = 3.3$ Hz), 8.59(1H, d, $J = 8.7$ Hz), 8.64(1H, d, $J = 6.0$ Hz).

IR (KBr) cm^{-1} : 3373, 1774, 1600, 1540, 1498, 1457, 1392, 1363, 1321, 1286, 1184, 1127, 1082, 1033.

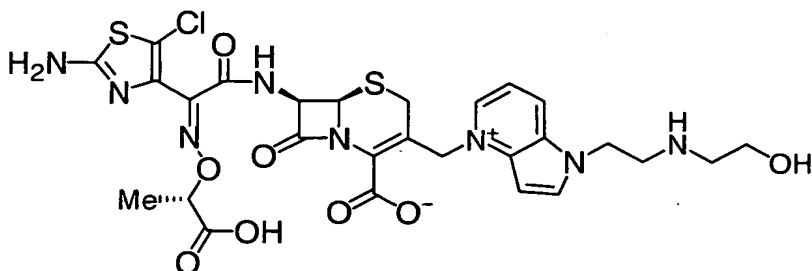
MS(FAB): 719 $^+$ ($\text{M}+\text{H}^+$).

Elementary Analysis as $\text{C}_{28}\text{H}_{31}\text{ClN}_{10}\text{O}_7\text{S}_2 \cdot 4.3 \text{ H}_2\text{O}$.

25 Calculated : C, 42.21 ; H, 5.01 ; N, 17.58 ; Cl, 4.45 ; S, 8.05 (%).

Found : C,42.28 ; H,4.87 ; N,17.55 ; Cl,4.19 ; S,7.84 (%).

Example 170



5 $^1\text{H-NMR}$ (D_2O) δ : 1.43(3H, d, $J = 7.2$ Hz), 3.17 and 3.38(2H, ABq, $J = 17.7$ Hz), 3.22(2H, m), 3.69(2H, t, $J = 6.3$ Hz), 3.81(2H, m), 4.65(1H, q, $J = 7.2$ Hz), 4.83(2H, t, $J = 6.3$ Hz), 5.18(1H, d, $J = 4.8$ Hz), 5.57 and 5.71(2H, ABq, $J = 15.0$ Hz), 5.86(1H, d, $J = 4.8$ Hz), 7.10(1H, d, $J = 3.3$ Hz), 7.74(1H, dd, $J = 6.0$ and 8.4 Hz), 8.16(1H, d, $J = 3.3$ Hz), 8.64(1H, d, $J = 8.4$ Hz), 8.69(1H, d, $J = 6.0$ Hz).

10 IR (KBr) cm^{-1} : 3385, 1773, 1601, 1539, 1500, 1466, 1393, 1364, 1287, 1186, 1139, 1112, 1064, 1033.

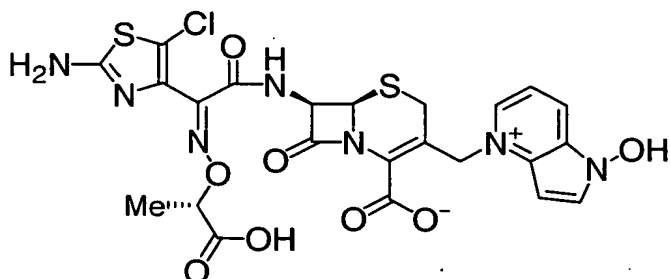
MS(FAB): 693 $^+$ (M+H $^+$).

Elementary Analysis as $\text{C}_{27}\text{H}_{29}\text{ClN}_8\text{O}_8\text{S}_2 \cdot 2.9 \text{H}_2\text{O}$.

Calculated : C,43.51 ; H,4.71 ; N,15.03 ; Cl,4.76 ; S,8.60 (%).

15 Found : C,43.61 ; H,4.80 ; N,15.12 ; Cl,4.48 ; S,8.21 (%).

Example 171



$^1\text{H-NMR}$ (D_2O) δ : 1.43(3H, d, $J = 7.2$ Hz), 3.19 and 3.28 (2H, ABq, $J = 18.0$ Hz), 4.64(1H, q, $J = 7.2$ Hz), 5.15(1H, d, $J = 4.8$ Hz), 5.41 and 5.65(2H, ABq, $J = 15.0$ Hz), 5.87(1H, d, $J = 4.8$ Hz), 6.58(1H, d, $J = 3.3$ Hz), 7.43(1H, dd, $J = 6.3$ and 8.1 Hz), 7.90(1H, d, $J = 3.3$ Hz), 8.37(1H, d, $J = 8.1$ Hz), 8.40(1H, d, $J = 6.3$ Hz).

IR (KBr) cm^{-1} : 3468, 3144, 3116, 3099, 3080, 2980, 2951, 2924, 2870, 2341,

2276, 2256, 1934, 1891, 1754, 1618, 1580, 1499, 1449, 1429, 1365, 1345,

25 1309, 1237, 1227, 1208, 1187, 1159, 1114, 1054.

MS(FAB): 622⁺(M+H⁺).

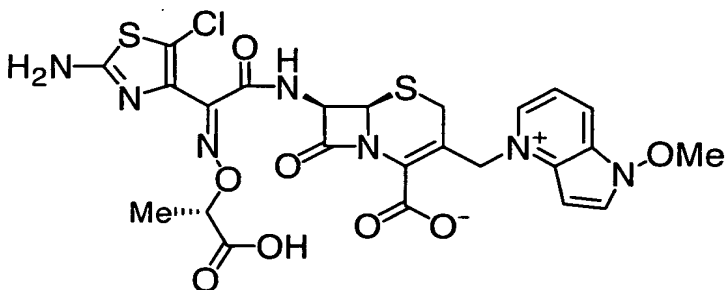
Elementary Analysis as C₂₃H₂₀ClN₇O₈S₂ · 3.5 H₂O.

Calculated : C,40.32 ; H,3.97 ; N,14.31 ; Cl,5.17 ; S,9.36 (%).

Found : C,40.38 ; H,3.90 ; N,14.23 ; Cl,5.36 ; S,9.25 (%).

5

Example 172



¹H-NMR (D₂O) δ : 1.44(3H, d, J = 6.9 Hz), 3.18 and 3.37 (2H, ABq, J = 17.4 Hz), 4.26(s, 3H), 4.65(1H, q, J = 6.9 Hz), 5.18(1H, d, J = 4.8 Hz), 5.55 and 5.71(2H, ABq, J = 15.3 Hz), 5.88(1H, d, J = 4.8 Hz), 6.91(1H, d, J = 3.6 Hz), 7.74(1H, dd, J = 6.3 and 8.1 Hz), 8.31(1H, d, J = 3.6 Hz), 8.65(1H, d, J = 8.1 Hz), 8.68(1H, d, J = 6.3 Hz).

IR (KBr) cm⁻¹: 3410, 3134, 2941, 1778, 1674, 1614, 1537, 1457, 1364, 1234, 1211, 1188, 1155, 1120, 1058, 1034.

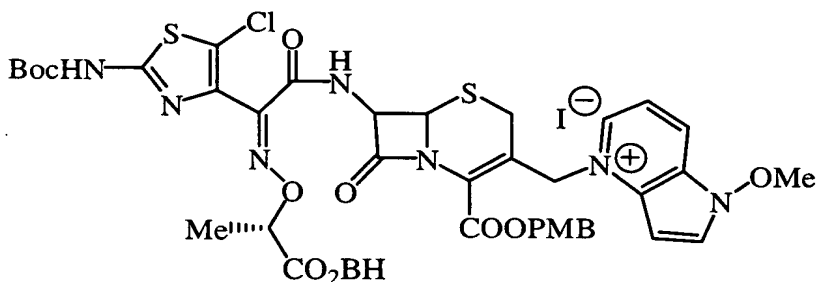
MS(ESI): 636⁺(M+H⁺).

Elementary Analysis as C₂₄H₂₂ClN₇O₈S₂ · 3.2 H₂O.

Calculated : C,41.55 ; H,4.13 ; N,14.13 ; Cl,5.11 ; S,9.24 (%).

Found : C,41.62 ; H,4.21 ; N,14.26 ; Cl,4.90 ; S,9.08 (%).

quaternary salt ester :



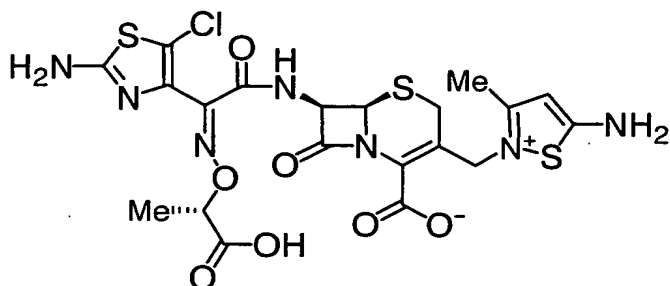
¹H-NMR (d₆-DMSO) δ : 1.44(3H, d, J = 6.9 Hz), 1.46(9H, s), 3.34 and 3.42(2H, Abq, J = 18.0 Hz), 3.76(3H, s), 4.26(3H, s), 4.89(1H, q, J = 6.9 Hz), 5.19(1H, d, J = 5.1 Hz), 5.22 and 5.29(2H, Abq, J = 11.7 Hz), 5.68 and 5.75(2H, Abq, J = 15.3 Hz), 5.97(1H, dd, J = 5.1 and 8.4 Hz), 6.82(1H, s), 6.89(2H, d, J = 9.0 Hz), 6.95(1H, d, J = 3.6 Hz), 7.20-7.42(12H, m), 7.84(1H, dd, J = 6.0 and 8.1 Hz), 8.67(1H, d, J = 6.0 Hz), 8.73(1H, d, J = 3.6 Hz), 8.86(1H, d, J = 8.1 Hz), 9.76(1H, d, J = 8.4 Hz), 12.1(brs).

IR (KBr) cm^{-1} : 3394, 3131, 3091, 3061, 3031, 2978, 2937, 1789, 1719, 1632, 1613, 1549, 1515, 1495, 1455, 1391, 1368, 1247, 1176, 1154, 1119, 1063, 1032.

MS(FAB): 1222 $^{+}$ ($\text{C}_{50}\text{H}_{49}\text{ClN}_7\text{O}_{11}\text{S}_2^{+}$).

5

Example 173



$^1\text{H-NMR}$ (D_2O) δ : 1.47(3H, d, $J = 6.9$ Hz), 2.43(3H, s), 3.26 and 3.62 (2H, ABq, $J = 17.7$ Hz), 4.66(1H, q, $J = 6.9$ Hz), 4.79 and 4.95(2H, ABq, $J = 14.7$ Hz), 5.26(1H, d, $J = 4.8$ Hz), 5.88(1H, d, $J = 4.8$ Hz), 6.26(1H, s).

10

IR (KBr) cm^{-1} : 3312, 3190, 1776, 1671, 1617, 1535, 1460, 1392, 1337, 1187, 1134, 1100, 1064, 1034.

MS(FAB): 602 $^{+}$ ($\text{M}+\text{H}^{+}$).

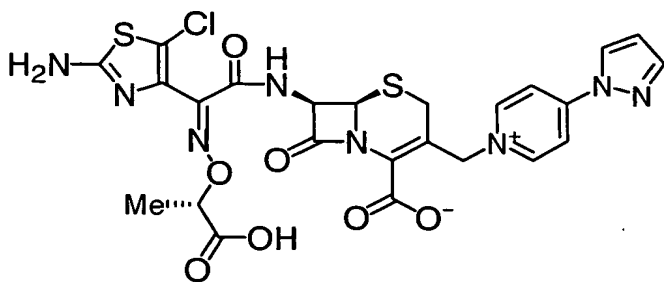
Elementary Analysis as $\text{C}_{20}\text{H}_{20}\text{ClN}_7\text{O}_7\text{S}_3 \cdot 2.5 \text{H}_2\text{O}$.

Calculated: C, 37.12; H, 3.89; N, 15.15; Cl, 5.48; S, 14.87 (%).

15

Found: C, 36.94; H, 3.98; N, 14.93; Cl, 5.42; S, 15.09 (%).

Example 174



$^1\text{H-NMR}$ (D_2O) δ : 1.44(3H, d, $J = 7.2$ Hz), 3.26 and 3.66(2H, ABq, $J = 18.0$ Hz), 4.64(1H, q, $J = 7.2$ Hz), 5.25 and 5.50(2H, ABq, $J = 14.4$ Hz), 5.28(1H, d, $J = 4.8$ Hz), 5.89(1H, d, $J = 4.8$ Hz), 6.78(1H, dd, $J = 1.8$ and 3.0 Hz), 8.04(1H, d, $J = 1.8$ Hz), 8.27 and 8.94(2H, ABq, $J = 7.2$ Hz), 8.53(1H, d, $J = 3.0$ Hz).

IR (KBr) cm^{-1} : 3417, 3135, 1779, 1673, 1639, 1537, 1480, 1446, 1397, 1360,

1217, 1159, 1116, 1036.

25

MS(FAB): 633⁺(M+H⁺).

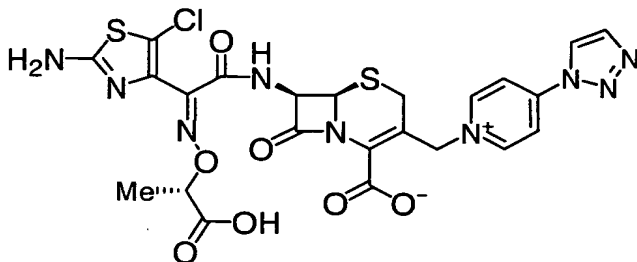
Elementary Analysis as C₂₄H₂₁ClN₈O₇S₂ · 2.7 H₂O.

Calculated : C,42.29 ; H,3.90 ; N,16.44 ; Cl,5.20 ; S,9.41 (%).

Found : C,42.41 ; H,3.97 ; N,16.42 ; Cl,4.93 ; S,9.24 (%).

5

Example 175



¹H-NMR (D₂O) δ : 1.44(3H, d, J = 6.9 Hz), 3.28 and 3.70(2H, ABq, J = 18.0 Hz), 4.65(1H, q, J = 6.9 Hz), 5.30(1H, d, J = 5.1 Hz), 5.36 and 5.63(2H, ABq, J = 14.7 Hz), 5.92(1H, d, J = 5.1 Hz), 8.07(1H, d, J = 1.8 Hz), 8.59 and 9.18(2H, ABq, J = 7.5 Hz), 8.85(1H, d, J = 1.8 Hz).

IR (KBr) cm⁻¹: 3415, 3132, 1778, 1673, 1638, 1530, 1475, 1341, 1247, 1186, 1159, 1125, 1095, 1064, 1032.

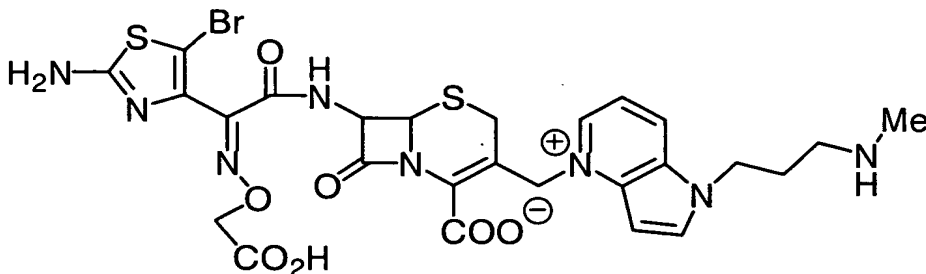
MS(FAB): 634⁺(M+H⁺).

15 Elementary Analysis as C₂₃H₂₀ClN₉O₇S₂ · 2.6 H₂O.

Calculated : C,40.57 ; H,3.73 ; N,18.51 ; Cl,5.21 ; S,9.42 (%).

Found : C,40.61 ; H,3.67 ; N,18.52 ; Cl,4.96 ; S,9.20 (%).

Example 176



¹H-NMR (D₂O) δ : 2.30(2H, m), 2.67(3H, s), 3.054(2H, m), 3.15 and 3.38 (2H, ABq, J = 17.7 Hz), 4.52(2H, t, J = 6.6 Hz), 4.55(2H, s), 5.17(1H, d, J = 4.8 Hz), 5.56 and 5.67(2H, ABq, J = 15.0 Hz), 5.85(1H, d, J = 4.8 Hz), 7.04(1H, d, J = 3.3 Hz), 7.68(1H, dd, J = 6.3 and 8.1 Hz), 8.11(1H, d, J = 3.3 Hz), 8.59(1H, d, J = 8.1 Hz), 8.64(1H, d, J = 6.3 Hz).

IR (KBr) cm⁻¹: 3418, 1771, 1607, 1534, 1497, 1466, 1391, 1360, 1317, 1152,

1119, 1052, 1020.

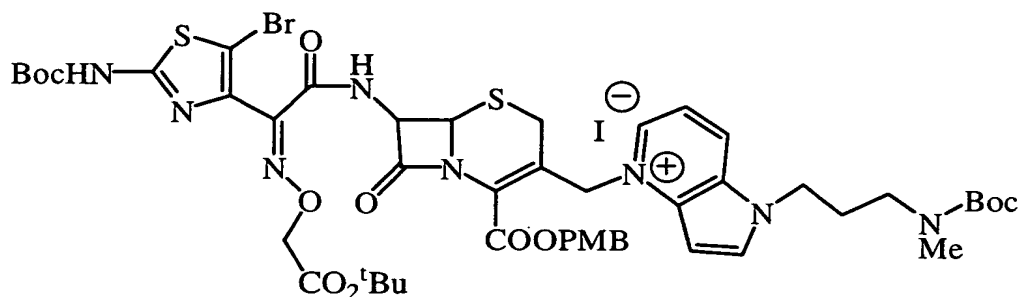
MS(ESI): 707⁺(M+H⁺).

Elementary Analysis as C₂₆H₂₇BrN₈O₇S₂ · 5.4 H₂O.

Calculated : C,38.80 ; H,4.73 ; N,13.92 ; Br,9.93; S,7.97 (%).

5 Found : C,38.80 ; H,4.46 ; N,14.04 ; Br,9.66; S,8.01 (%).

quaternary salt ester :



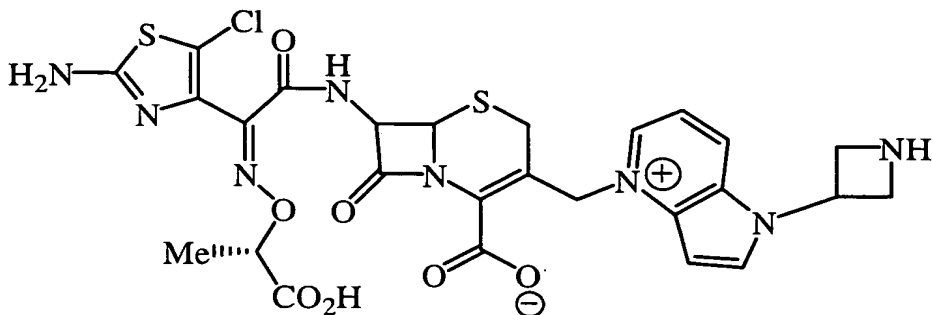
¹H-NMR (d₆-DMSO) δ : 1.40(9H, s), 1.46(18H, s), 2.03(2H, m), 2.78(3H, brs), 3.18(2H, t, J = 6.6 Hz), 3.26 and 3.43(2H, Abq, J = 18.3 Hz), 3.75(3H, s), 4.43(2H, t-like), 4.55(2H, s), 5.17(1H, d, J = 4.8 Hz), 5.21 and 5.28(2H, Abq, J = 11.7 Hz), 5.65 and 5.73(2H, ABq, J = 15.0 Hz), 5.94(1H, dd, J = 4.8 and 8.7 Hz), 6.88 and 7.32(4H, Abq, J = 8.7 Hz), 7.00(1H, d, J = 3.3 Hz), 7.79(1H, dd, J = 6.0 and 8.1 Hz), 8.43(1H, d, J = 3.3 Hz), 8.60(1H, d, J = 6.0 Hz), 8.88(1H, d, J = 8.1 Hz), 9.61(1H, d, J = 8.7 Hz), 12.1(brs).

IR (KBr) cm⁻¹: 3428, 3060, 2976, 2933, 1790, 1720, 1686, 1630, 1613, 1584,

1548, 1515, 1496; 1455, 1393, 1368, 1300, 1247, 1156, 1078, 1062, 1024.

MS(ESI): 1083⁺(C₄₈H₆₀BrN₈O₁₂S₂⁺).

Example 177



20 ¹H-NMR (D₂O) δ : 1.43(3H, d, J = 6.9 Hz), 3.17 and 3.38(2H, ABq, J = 17.7 Hz), 4.65(1H, q, J = 6.9 Hz), 4.70-4.75(4H, m), 5.18(1H, d, J = 4.8 Hz), 5.57 and 5.71(2H, ABq, J = 15.3 Hz), 5.86(1H, d, J = 4.8 Hz), 5.95(1H, quintet-like), 7.20(1H, d, J = 3.6 Hz), 7.73(1H, dd, J = 6.3 and 8.4 Hz), 8.53(1H, d, J = 3.6 Hz), 8.60(1H, d, J = 8.4 Hz), 8.70(1H, d, J = 6.3 Hz).

IR (KBr) cm^{-1} : 3407, 2985, 2670, 1773, 1604, 1539, 1502, 1463, 1394, 1364, 1286, 1185, 1136, 1090, 1064, 1032.

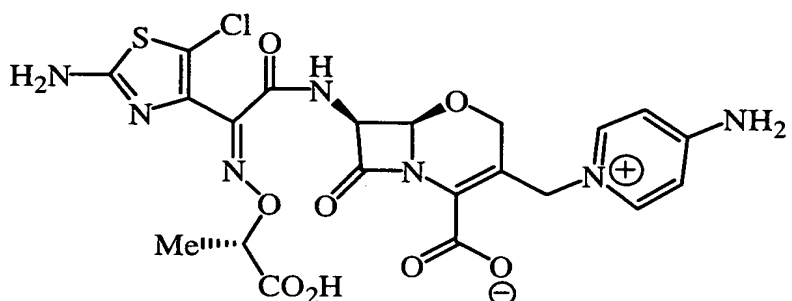
MS(FAB): 661⁺(M+H⁺) .

Elementary Analysis as $\text{C}_{26}\text{H}_{25}\text{ClN}_8\text{O}_7\text{S}_2 \cdot 4.5 \text{ H}_2\text{O}$.

5 Calculated : C, 42.08 ; H, 4.62 ; N, 15.10 ; Cl, 4.78 ; S, 8.64 (%).

Found : C, 42.05 ; H, 4.60 ; N, 15.23 ; Cl, 4.50 ; S, 8.34 (%).

Example 178



10 ¹H-NMR (D₂O) δ : 1.37(3H, d, J = 6.9 Hz), 4.34 and 4.41(2H, ABq, J = 17.4 Hz), 4.61(1H, q, J = 6.9 Hz), 4.87 and 5.21(2H, ABq, J = 14.7 Hz), 5.31(1H, d, J = 3.9 Hz), 5.65(1H, d, J = 3.9 Hz), 6.83 and 8.08(2H, ABq, J = 7.2 Hz).

IR (KBr) cm^{-1} : 3344, 3197, 1781, 1655, 1538, 1444, 1402, 1372, 1349, 1279, 1240, 1210, 1171, 1109, 1064, 1034.

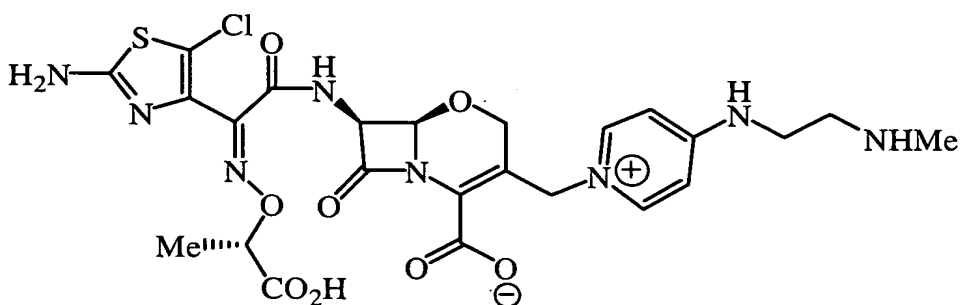
15 MS(FAB): 566⁺(M+H⁺)

Elementary Analysis as $\text{C}_{21}\text{H}_{20}\text{ClN}_7\text{O}_8\text{S} \cdot 3.0 \text{ H}_2\text{O}$.

Calculated : C, 40.68 ; H, 4.23 ; N, 15.81 ; Cl, 5.72 ; S, 5.17 (%).

Found : C, 40.56 ; H, 3.90 ; N, 15.83 ; Cl, 5.84 ; S, 5.18 (%).

Example 179



20

¹H-NMR (D₂O) δ : 1.38(3H, d, J = 7.2 Hz), 3.33(2H, t, J = 6.0 Hz), 3.73(2H, t, J = 6.0 Hz), 4.34 and 4.45(2H, ABq, J = 17.4 Hz), 4.63(1H, q, J = 7.2 Hz), 4.78 and 5.32(2H, ABq, J = 14.7 Hz), 5.33(1H, d, J = 3.9 Hz), 5.63(1H, d, J = 3.9 Hz), 6.83(2H, d-like),

8.08(2H, m).

IR (KBr) cm^{-1} : 3396, 3067, 1779, 1649, 1601, 1556, 1448, 1403, 1371, 1350, 1279, 1217, 1171, 1107, 1063, 1033.

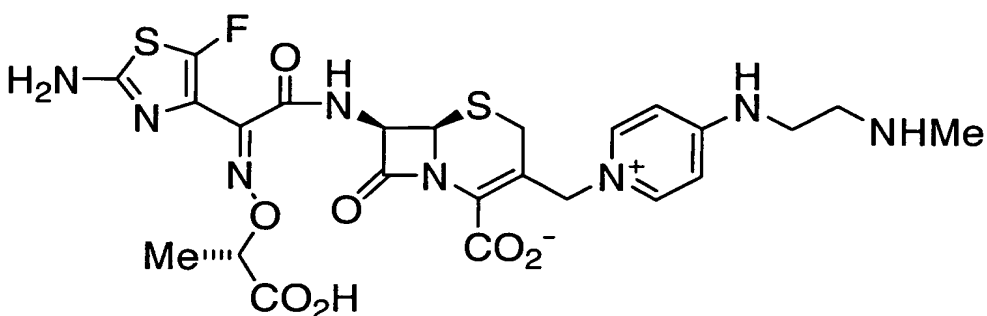
MS(FAB): 623⁺(M+H⁺).

5 Elementary Analysis as $\text{C}_{24}\text{H}_{27}\text{ClN}_8\text{O}_8\text{S} \cdot 4.9 \text{ H}_2\text{O}$.

Calculated : C, 40.52 ; H, 5.21 ; N, 15.75 ; Cl, 4.98 ; S, 4.51 (%).

Found : C, 40.36 ; H, 4.96 ; N, 15.90 ; Cl, 5.12 ; S, 4.67 (%).

Example 180



¹H-NMR (D₂O) δ : 1.31 (3H, d, J = 7.2 Hz), 2.64 (3H, s), 3.03 (1H, d, J = 17.1 Hz), 3.21 (2H, t, J = 6.0 Hz), 3.45 (1H, d, J = 17.1 Hz), 3.61 (2H, t, J = 6.0 Hz), 4.51 (1H, q, J = 7.2 Hz), 4.76 (1H, d, J = 15.0 Hz), 4.97 (1H, d, J = 15.0 Hz), 5.10 (1H, d, J = 4.2 Hz), 5.70 (1H, d, J = 4.2 Hz), 6.81 (2H, d, J = 6.3 Hz), 8.01-8.13 (2H, m).

15 IR (KBr) cm^{-1} : 3388, 3066, 1773, 1650, 1590, 1557, 1533, 1450, 1394, 1355, 1320, 1289, 1217, 1169, 1094, 1064, 1036.

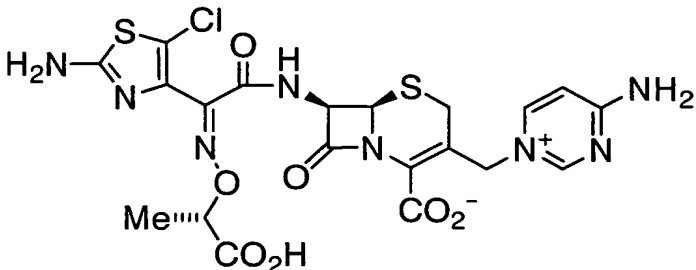
MS(FAB): 623⁺(M+H⁺) .

Elementary Analysis as $\text{C}_{24}\text{H}_{27}\text{FN}_8\text{O}_7\text{S}_2 \cdot 3.8 \text{ H}_2\text{O}$.

Calculated : C, 41.71; H, 5.05; N, 16.21; F, 2.75; S, 9.28 (%).

20 Found : C, 41.69; H, 4.92 ; N, 16.23; F, 2.51; S, 9.05 (%).

Example 181



¹H-NMR (D₂O) δ : 1.52 (3H, d, J = 6.9 Hz), 3.25 (1H, d, J = 17.7 Hz), 3.63 (1H, d, J =

(2H, t, J = 5.7 Hz), 3.53 (1H, d, J = 18.0 Hz), 3.82 (2H, t, J = 5.7 Hz), 4.54 (1H, q, J = 6.9 Hz), 4.75 (1H, d, J = 14.7 Hz), 4.96 (1H, d, J = 14.7 Hz), 5.13 (1H, d, J = 5.1 Hz), 5.74 (1H, d, J = 5.1 Hz), 6.77 (1H, d, J = 7.5 Hz), 8.12 (1H, br d, J = 7.5 Hz), 8.70 (1H, br s).

IR (KBr) cm^{-1} : 3409, 1775, 1652, 1605, 1538, 1509, 1447, 1394, 1370,

5 1287, 1170, 1095, 1065, 1035.

MS (FAB): 640 (M+H)⁺, 1279 (2M+H)⁺.

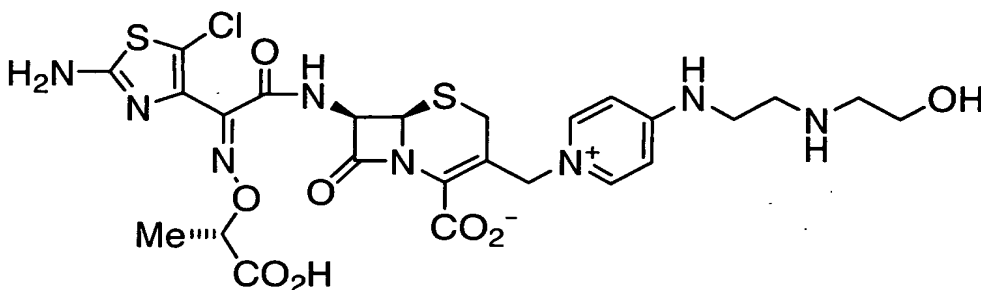
Elementary Analysis as $\text{C}_{23}\text{H}_{26}\text{ClN}_9\text{O}_7\text{S}_2 \cdot 3.5 \text{H}_2\text{O}$.

Calculated : C, 39.29; H, 4.73; N, 17.93; Cl, 5.04; S, 9.12 (%).

Found : C, 39.43; H, 4.68; N, 17.74; Cl, 5.00; S, 8.95 (%).

10

Example 184



¹H-NMR (D₂O) δ : 1.45 (3H, d, J = 6.9 Hz), 3.17 (1H, d, J = 18.0 Hz), 3.24 (2H, t, J = 5.1 Hz), 3.39 (2H, t, J = 6.3 Hz), 3.57 (1H, d, J = 18.0 Hz), 3.77 (2H, t, J = 6.3 Hz), 3.85 (2H, t, J = 5.1 Hz), 4.66 (1H, q, J = 6.9 Hz), 4.88 (1H, d, J = 15.0 Hz), 5.09 (1H, d, J = 15.0 Hz), 5.24 (1H, d, J = 4.8 Hz), 5.86 (1H, d, J = 4.8 Hz), 6.94 (2H, d, J = 6.9 Hz), 8.19 (2H, m).

IR (KBr) cm^{-1} : 3378, 1774, 1650, 1598, 1556, 1448, 1394, 1358, 1286,

1218, 1168, 1093, 1066, 1034.

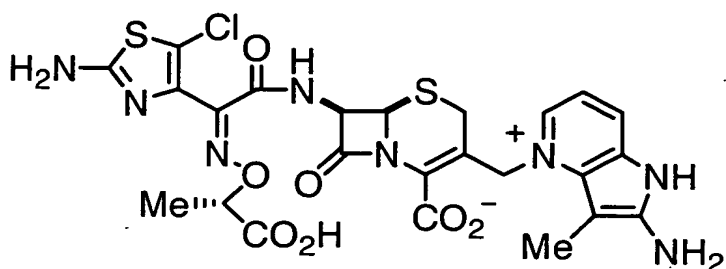
20 MS (FAB): 669 (M+H)⁺.

Elementary Analysis as $\text{C}_{25}\text{H}_{29}\text{ClN}_8\text{O}_8\text{S}_2 \cdot 2.7 \text{H}_2\text{O}$.

Calculated : C, 41.83; H, 4.83; N, 15.61; Cl, 4.94; S, 8.93 (%).

Found : C, 41.76; H, 4.61; N, 15.80; Cl, 4.78; S, 8.65 (%).

25 Example 185



¹H-NMR (d₆-DMSO) δ : 1.39 (3H, d, J = 6.9 Hz), 2.21 (3H, brs), 2.97 and 3.48 (2H, ABqt, J = 17.7 Hz), 4.57 (1H, q, J = 6.9 Hz), 5.09 (1H, d, J = 4.8 Hz), 5.41 (2H, brs), 5.77 (1H, dd, J = 4.8, 8.4 Hz), 6.75 (1H, t-like), 7.37-7.39 (3H, m), 7.70 (2H, brs), 8.05 (1H, d, J = 5.4 Hz), 9.96 (1H, brs), 13.5 (1H, brs).

IR (KBr) cm⁻¹: 3339, 3195, 1773, 1646, 1603, 1567, 1479, 1424, 1394, 1338, 1286, 1227, 1190, 1161, 1094, 1035.

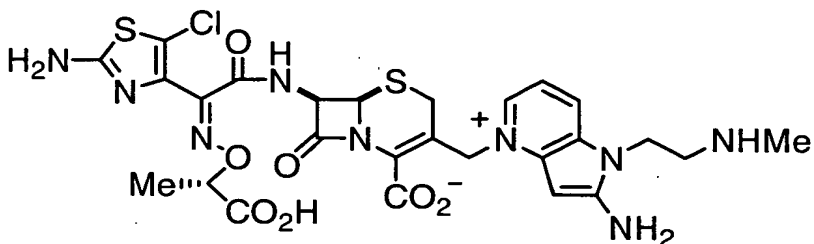
MS(FAB): 635⁺ (M+H)⁺.

Elementary Analysis as C₂₄H₂₃ClN₈O₇S₂ · 2.3 H₂O.

Calculated : C, 42.61; H, 4.11; N, 16.56; Cl, 5.24; S, 9.48 (%).

Found : C, 42.72; H, 4.27; N, 16.53; Cl, 5.02; S, 9.13 (%).

Example 186



¹H-NMR (D₂O + DCl) δ : 1.54 (3H, d, J = 7.5 Hz), 2.76 (3H, s), 3.24 and 3.46 (2H, ABqt, J = 18.6 Hz), 3.51 (2H, t, J = 6.3 Hz), 4.56 (2H, t, J = 6.3 Hz), 4.98 (1H, q, J = 7.5 Hz), 5.27 (1H, d, J = 4.8 Hz), 5.36 and 5.49 (2H, ABq, J = 15.9 Hz), 5.91 (1H, d, J = 4.8 Hz), 7.11 (1H, dd, J = 6.3, 7.8 Hz), 7.80 (1H, d, J = 7.8 Hz), 7.95 (1H, d, J = 6.3 Hz).

IR (KBr) cm⁻¹: 3369, 2457, 1761, 1646, 1564, 1475, 1435, 1398, 1360, 1317, 1284, 1191, 1164, 1092, 1036.

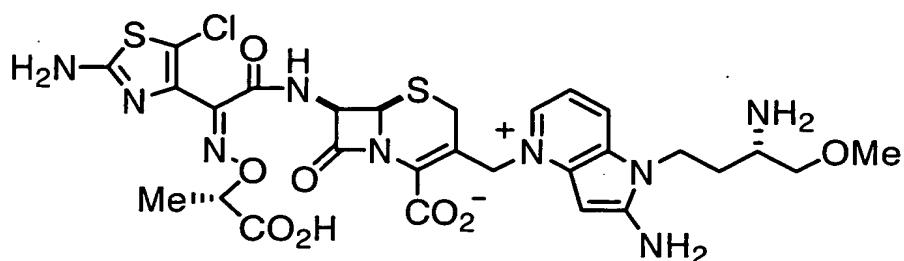
MS(FAB): 678⁺ (M+H)⁺.

Elementary Analysis as C₂₆H₂₈ClN₉O₇S₂ · 3.2 H₂O.

Calculated : C, 42.44; H, 4.71; N, 17.13; Cl, 4.82; S, 8.72 (%).

Found : C, 42.15; H, 4.41; N, 17.15; Cl, 4.86; S, 8.68 (%).

Example 187



¹H-NMR (D₂O + DCl) δ : 1.55 (3H, d, J = 6.9 Hz), 2.16–2.24 (3H, m), 3.37 (1H, d, J = 18.3 Hz), 3.43 (3H, s), 3.57–3.76 (4H, m), 4.31 (2H, t, J = 8.1 Hz), 4.79 (1H, d, J = 5.1 Hz), 4.99 (1H, q, J = 6.9 Hz), 5.49 and 5.68 (2H, ABq, J = 15.0 Hz), 5.92 (1H, d, J = 5.1 Hz), 7.35 (1H, dd, J = 6.6, 7.8 Hz), 7.97 (1H, d, J = 7.8 Hz), 8.14 (1H, d, J = 6.6 Hz).

IR (KBr) cm⁻¹: 3378, 3183, 1773, 1650, 1565, 1495, 1441, 1395, 1352, 1316, 1287, 1223, 1165, 1095, 1034.

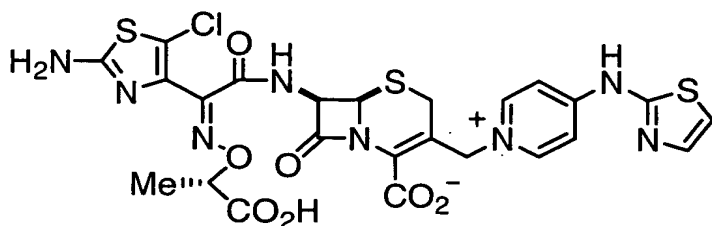
MS(FAB): 723⁺ (M+H)⁺

Elementary Analysis as C₂₇H₃₁ClN₁₀O₈S₂ · 2.6 H₂O.

Calculated : C,42.11; H,4.74 ; N,18.19 ; Cl,4.60; S,8.33 (%).

Found : C,42.14 ; H,4.54 ; N,18.19 ; Cl,4.50; S,8.16 (%).

Example 188



¹H-NMR (d₆-DMSO) δ : 1.39 (3H, d, J = 6.9 Hz), 3.07 and 3.49 (2H, d, J = 17.7 Hz), 4.56 (1H, q, J = 6.9 Hz), 4.92 and 5.38 (2H, ABq, J = 13.5 Hz), 5.07 (1H, d, J = 5.4 Hz), 5.73 (1H, dd, J = 5.4, 9.0 Hz), 7.35 (1H, d, J = 3.3 Hz), 7.40 (2H, brs), 7.54 (1H, d, J = 3.3 Hz), 8.05 (2H, brs), 8.90 (2H, brd, J = 7.2 Hz), 9.70 (1H, brs).

IR (KBr) cm⁻¹: 3416, 2984, 1777, 1643, 1547, 1515, 1476, 1461, 1348, 1204, 1161, 1102, 1063, 1036.

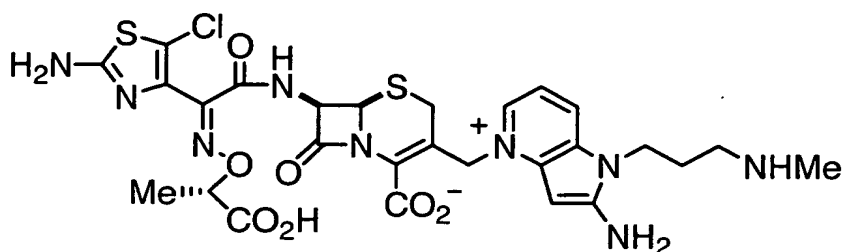
MS(FAB): 665⁺ (M+H)⁺.

Elementary Analysis as C₂₄H₂₁ClN₈O₇S₃ · 2.5H₂O.

Calculated : C,40.59; H,3.69; N,15.78; Cl,4.99; S,13.55 (%).

Found : C,40.41 ; H,3.62; N,16.01 ; Cl,5.03; S,13.25 (%).

Example 189



¹H-NMR (D₂O + DCl) δ : 1.54 (3H, d, J = 6.9 Hz), 2.14-2.24 (2H, m), 2.71 (3H, s), 3.11 (2H, t, J = 8.4 Hz), 3.25 and 3.48 (2H, ABqt, J = 18.3 Hz), 4.28 (2H, t, J = 7.5 Hz), 4.99 (1H, q, J = 6.9 Hz), 5.29 (1H, d, J = 4.8 Hz), 5.34 and 5.51 (2H, ABq, J = 15.6 Hz), 5.91 (1H, d, J = 4.8 Hz), 7.08 (1H, dd, J = 6.6, 7.5 Hz), 7.78 (1H, d, J = 7.5 Hz), 7.91 (1H, d, J = 6.6 Hz).

IR (KBr) cm⁻¹: 3341, 3177, 1772, 1646, 1564, 1473, 1439, 1394, 1346, 1284, 1190, 1162, 1092, 1058, 1034.

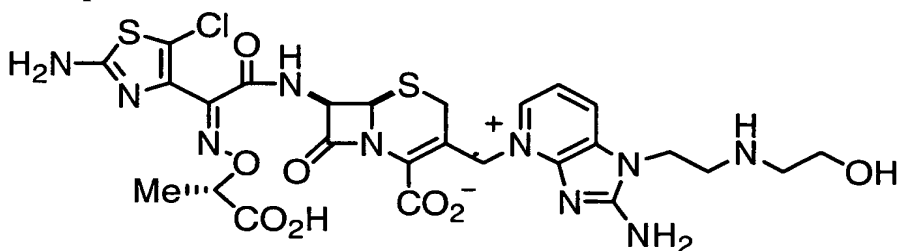
MS(FAB): 692⁺ (M+H)⁺.

Elementary Analysis as C₂₇H₃₀ClN₉O₇S₂ · 3.8 H₂O.

10 Calculated : C,42.63; H,4.98 ; N,16.57 ; Cl,4.66; S,8.43 (%).

Found : C,42.69 ; H,4.81 ; N,16.49 ; Cl,4.67; S,8.51 (%).

Example 190



15 ¹H-NMR (D₂O+DCl) δ : 1.55 (3H, d, J = 6.9 Hz), 3.27 (2H, t, J = 8.3 Hz), 3.36 and 3.59 (2H, ABq, J = 18.3 Hz), 3.61 (2H, t, J = 6.8 Hz), 3.86 (2H, t, J = 8.3 Hz), 4.98 (1H, sept, J = 6.9 Hz), 5.27 (1H, d, J = 4.8 Hz), 5.47 and 5.70 (2H, ABq, J = 15.2 Hz), 7.32-7.38 (1H, m), 8.01 (1H, d, J = 7.5 Hz), 8.16 (1H, d, J = 6.9 Hz).

20 IR (KBr) cm⁻¹:3371, 3184, 1772, 1667, 1603, 1563, 1395, 1351, 1316, 1222, 1170, 1072, 1034, 984, 867, 758.

MS(FAB): 709⁺ (M+H)⁺.

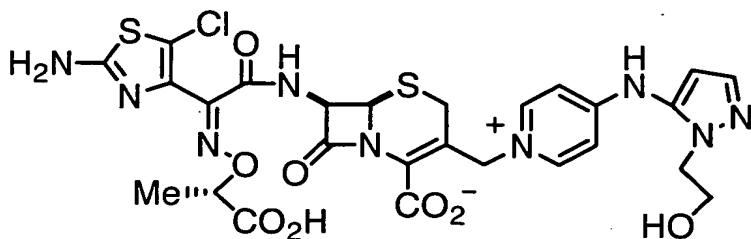
Elementary Analysis as C₂₆H₂₉ClN₁₀O₈S₂ · 2.6 H₂O.

Calculated : C,41.31 ; H,4.56 ; N,18.53 ; Cl,4.69; S,8.48 (%).

Found : C,41.22 ; H,4.37 ; N,18.51 ; Cl,5.27; S,8.25 (%).

25

Example 191



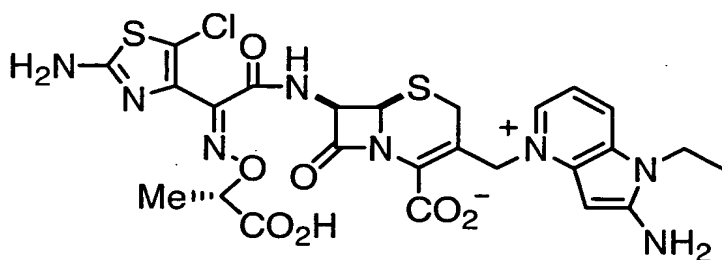
¹H-NMR (d₆-DMSO) δ : 1.39 (3H, d, J = 6.9 Hz), 3.04 and 3.486 (2H, ABqt, J = 17.4 Hz), 3.67 (2H, t, J = 5.4 Hz), 4.07 (2H, t, J = 5.4 Hz), 4.57 (1H, q, J = 6.9 Hz), 4.84 and 5.30 (2H, ABq, J = 13.8 Hz), 5.06 (1H, d, J = 4.8 Hz), 5.72 (1H, dd, J = 4.8, 8.7 Hz), 6.31 (1H, d, J = 1.8 Hz), 7.14 (2H, brs), 7.41 (2H, brs), 7.57 (1H, d, J = 1.8 Hz), 8.72 (1H, d, J = 7.2 Hz), 9.65 (1H, brs), 10.8 (1H, brs).
 IR (KBr) cm⁻¹: 3308, 2948, 1777, 1648, 1608, 1541, 1456, 1357, 1212, 1165, 1109, 1065, 1036.
 MS(FAB): 692⁺ (M+H)⁺.

Elementary Analysis as C₂₆H₂₆ClN₉O₈S₂ · 2.2 H₂O.

Calculated : C,42.68; H,4.19 ; N,17.23 ; Cl,4.84; S,8.78 (%).

Found : C,42.79 ; H,4.10 ; N,17.32 ; Cl,4.47; S,8.45 (%).

Example 192



¹H-NMR (d₆-DMSO) δ : 1.20 (3H, t, J = 6.9 Hz), 1.38 (3H, d, J = 7.2 Hz), 2.94 and 3.27 (2H, ABqt, J = 17.4 Hz), 4.16 (2H, q, J = 6.9 Hz), 4.55 (2H, q, J = 7.2 Hz), 5.00 (1H, d, J = 4.8 Hz), 5.22 and 5.34 (2H, ABq, J = 14.4 Hz), 5.68 (1H, dd, J = 4.8, 9.0 Hz), 6.05 (1H, s), 6.99 (1H, dd, J = 6.6, 7.5 Hz), 7.40 (2H, brs), 7.79 (1H, d, J = 7.5 Hz), 7.88 (2H, brs), 8.27 (1H, d, J = 6.6 Hz), 9.78 (1H, brs).

IR (KBr) cm⁻¹: 3346, 3189, 2985, 2936, 1777, 1646, 1594, 1563, 1474, 1441, 1386, 1342, 1285, 1191, 1162, 1098, 1036.

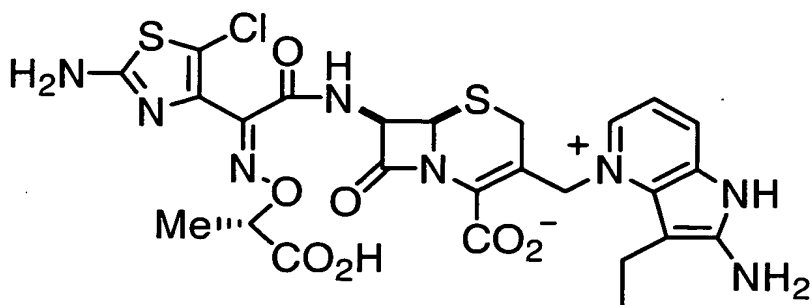
MS(FAB): 649⁺ (M+H)⁺.

Elementary Analysis as C₂₅H₂₅ClN₈O₇S₂ · 2.3 H₂O.

Calculated : C,43.48; H,4.32 ; N,16.23 ; Cl,5.13; S,9.29 (%).

Found : C,43.48 ; H,4.21 ; N,16.28 ; Cl,4.80; S,8.98 (%).

Example 193



¹H-NMR (d₆-DMSO) δ : 1.04 (3H, t, J = 7.2 Hz), 1.40 (3H, d, J = 6.9 Hz), 2.60-2.70 (2H, m), 2.97 and 3.49(2H, ABqt, J = 17.4 Hz), 4.57 (1H, q, J = 6.9 Hz), 5.10 (1H, d, J = 4.8 Hz), 5.24 and 5.46 (2H, ABq, J = 14.7 Hz), 5.78 (1H, dd, J = 4.8, 8.1 Hz), 6.75 (1H, t-like), 7.37-7.39 (3H, m), 7.72 (2H, brs), 8.00 (1H, brs), 9.92 (1H, brs), 13.1 (1H, brs).

IR (KBr) cm⁻¹: 3341, 3196, 2972, 2934, 1176, 1633, 1567, 1475, 1423, 1344, 1225, 1187, 1159, 1101, 1058, 1033.

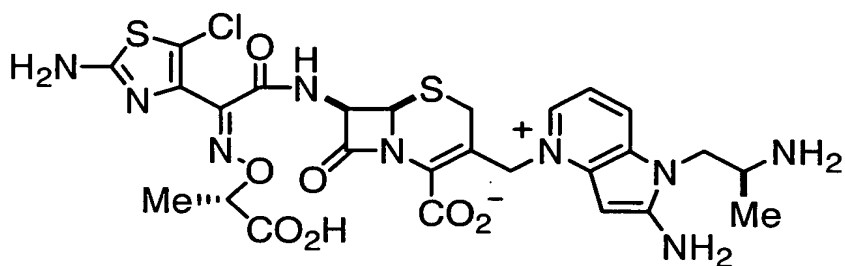
MS(FAB): 649⁺ (M+H)⁺.

10 Elementary Analysis as C₂₅H₂₅ClN₈O₇S₂ · 2.6H₂O.

Calculated : C,43.15; H,4.37 ; N,16.10 ; Cl,5.09; S,9.21 (%).

Found : C,43.25 ; H,4.18 ; N,16.06 ; Cl,4.81; S,8.86 (%).

Example 194



¹H-NMR (D₂O + DCl) δ : 1.41 (3H, d, J = 6.3 Hz), 1.54 (3H., d, J = 6.9 Hz), 3.26 and 3.49 (2H, ABqt, J = 18.3 Hz), 3.87-3.99 (1H, m), 4.35-4.49 (2H, m), 5.29 (1H, d, J = 4.8 Hz), 5.36 and 5.53 (2H, ABq, J = 15.3 Hz), 5.91 (1H, d, J = 4.8 Hz), 7.11 (1H, dd, J = 6.3, 7.8 Hz), 7.83 (1H, d, J = 7.8 Hz), 7.95 (1H, d, J = 6.3 Hz).

20 IR (KBr) cm⁻¹: 3353, 3176, 1756, 1647, 1561, 1436, 1398, 1355, 1318, 1284, 1236, 1165, 1092, 1036.

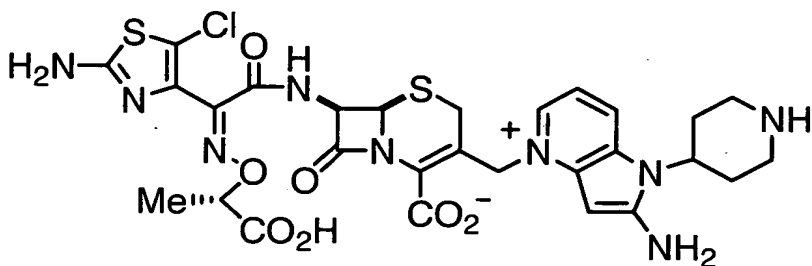
MS(FAB): 678⁺ (M+H)⁺.

Elementary Analysis as C₂₆H₂₉ClN₉O₇S₂ · 3.2 H₂O.

Calculated : C,42.38; H,4.84 ; N,17.11 ; Cl,4.81; S,8.70 (%).

25 Found : C,42.46 ; H,4.69 ; N,17.11 ; Cl,4.58; S,8.47 (%).

Example 195



¹H-NMR (D₂O+DCI) δ : 1.54 (3H, d, J = 6.9 Hz), 2.24 (3H, s), 2.26 (2H, d-like), 2.62-2.74 (2H, m), 3.19-3.34 (3H, m), 3.46 (1H, d, J = 18.3 Hz), 3.72 (2H, d-like), 4.69-4.78 (1H, m), 4.99 (1H, q, J = 6.9 Hz), 5.29 (1H, d, J = 4.8 Hz), 5.35 and 5.53 (2H, ABq, J = 15.6 Hz), 5.91 (1H, t-like), 7.08 (1H, t-like), 7.94 (2H, t-like).

IR (KBr) cm⁻¹: 3355, 3184, 1771, 1594, 1559, 1476, 1434, 1395, 1349, 1317, 1283, 1188, 1166, 1066, 1033, 1001.

MS(FAB): 704⁺ (M+H)⁺.

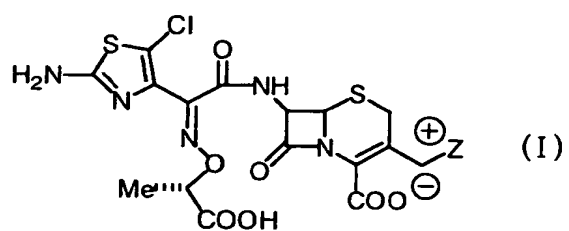
Elementary Analysis as C₂₈H₃₀ClN₉O₇S₂ · 3.6 H₂O.

Calculated : C,43.73 ; H,4.88 ; N,16.39 ; Cl,4.61 ; S,8.34 (%).

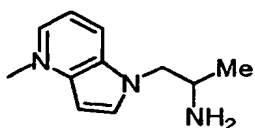
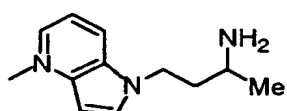
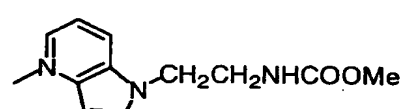
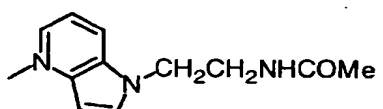
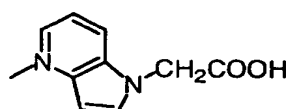
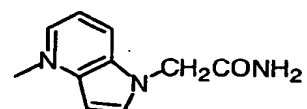
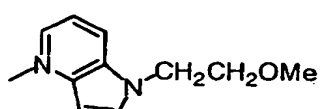
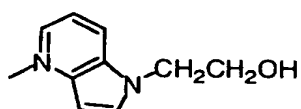
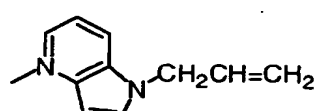
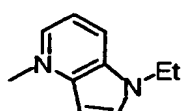
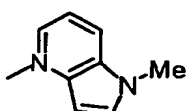
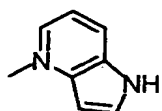
Found : C,43.74 ; H,4.65 ; N,16.50 ; Cl,4.40 ; S,8.13 (%).

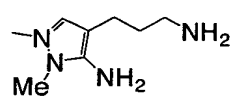
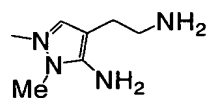
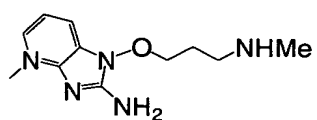
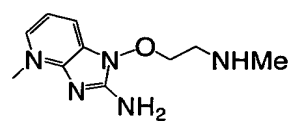
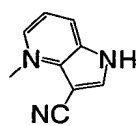
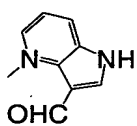
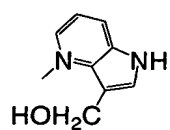
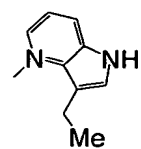
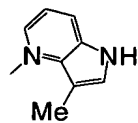
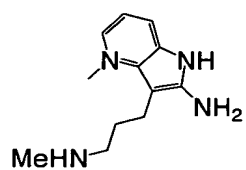
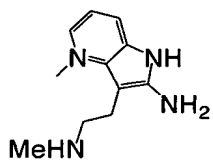
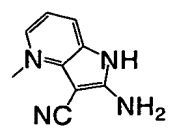
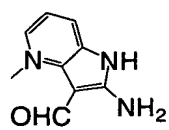
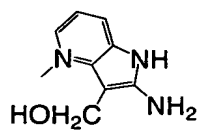
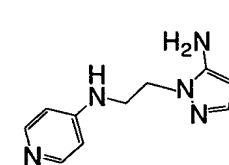
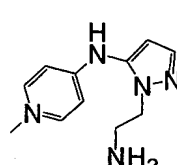
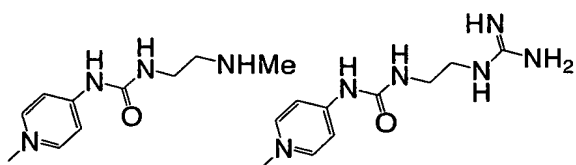
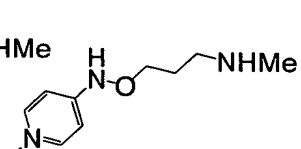
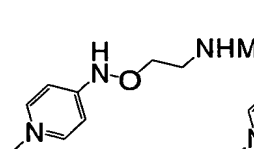
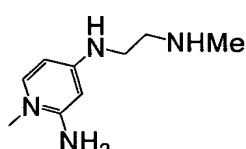
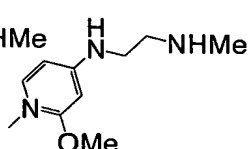
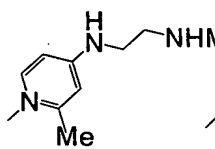
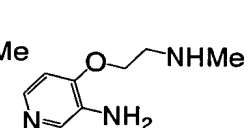
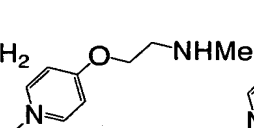
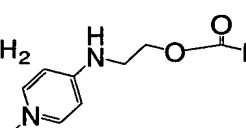
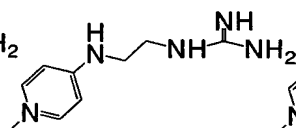
Example A

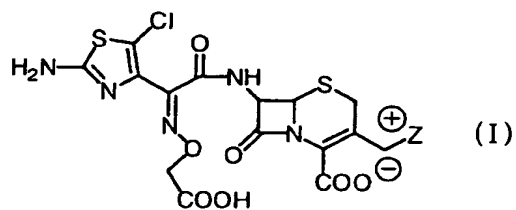
According to the above Examples, the following compound (I) is synthesized.



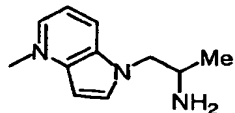
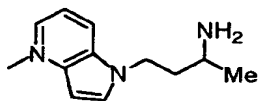
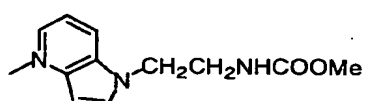
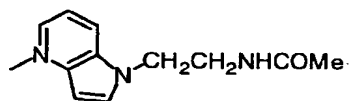
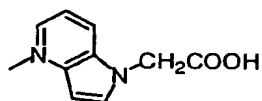
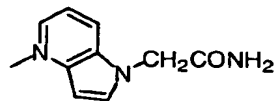
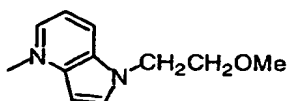
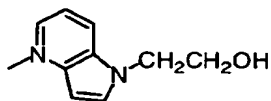
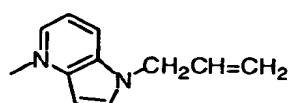
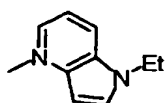
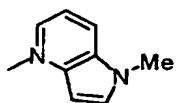
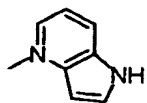
Z =



Nc1cnc2c(c1)cnc2N3CCCCC3NCCNc1ccncc1



Z =



Experiment 1

The MIC (minimum inhibitory concentration) value of the invention compounds
 5 against various bacterial was determined by the usual agar dilution method. The
 result is shown in Table 1.

(Table 1)

(unit: $\mu\text{g} / \text{ml}$)

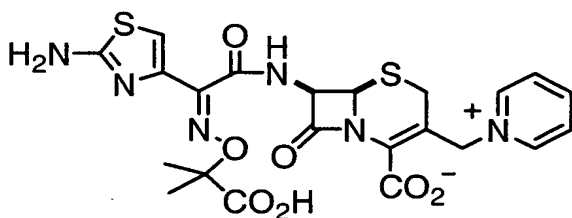
| Example No | S.aureus SR3637 (H-MRSA) *1 | S.epidermidis SR25009 (MRSE) *2 | E.cloacae SR4321 (Bla++) *3 | P.aeruginosa SR24-12 *3 |
|------------|-----------------------------|---------------------------------|-----------------------------|-------------------------|
| Ref. 1 | >128 | >128 | 64 | 64 |
| Ex. 1 | 64 | 32 | 16 | 8 |
| Ex. 3 | 32 | 32 | 16 | 8 |
| Ex. 4 | 16 | 8 | 4 | 8 |
| Ex. 5 | 16 | 8 | 8 | - |
| Ex. 8 | 32 | 32 | 4 | 4 |
| Ex. 9 | 16 | 8 | 2 | 4 |
| Ex. 18 | 8 | 4 | 2 | 4 |
| Ex. 19 | 16 | 8 | 1 | 8 |
| Ex. 20 | 16 | 16 | 8 | 4 |
| Ex. 79 | 8 | 8 | 2 | 4 |
| Ex. 98 | 8 | 8 | 2 | 2 |
| Ex. 124 | 16 | 8 | 4 | 4 |
| Ex. 132 | 16 | 8 | 4 | 4 |

*1 Methicillin High-Resistant Staphylococcus Aureus

*2 Methicillin High-Resistant Staphylococcus Epidermidis

5 *3 AmpC High-Production Cephem Resistant Strain

Ref 1



10 The above result shows that the invention compounds, having a substituent such as halogen on the aminothiazole ring, possesses a potent antibacterial activity against various bacteria including H-MRSA, H-MRSE and P.aeruginosa in comparison with Ref 1 compound, Ceftazidime.

15 Formulation Example 1

The invention compound of Example 1 and a pH adjusting agent are filled as powder to prepare an injection agent.

Industrial Utility

The invention compounds exhibit a potent antibacterial activity against various bacteria including Gram-positive bacteria and Gram-negative bacteria. In particular, the invention compounds are stable against β -lactamase and extremely efficacious against cephem-resistant bacteria including C-class β -lactamase-producing
5 *P.aeruginosa*. Further, the invention compounds have an excellent pharmacokinetics and a high water-solubility, thus preferably being suitable for an injection agent.